

FIGURE 1

BEST AVAILABLE COPY

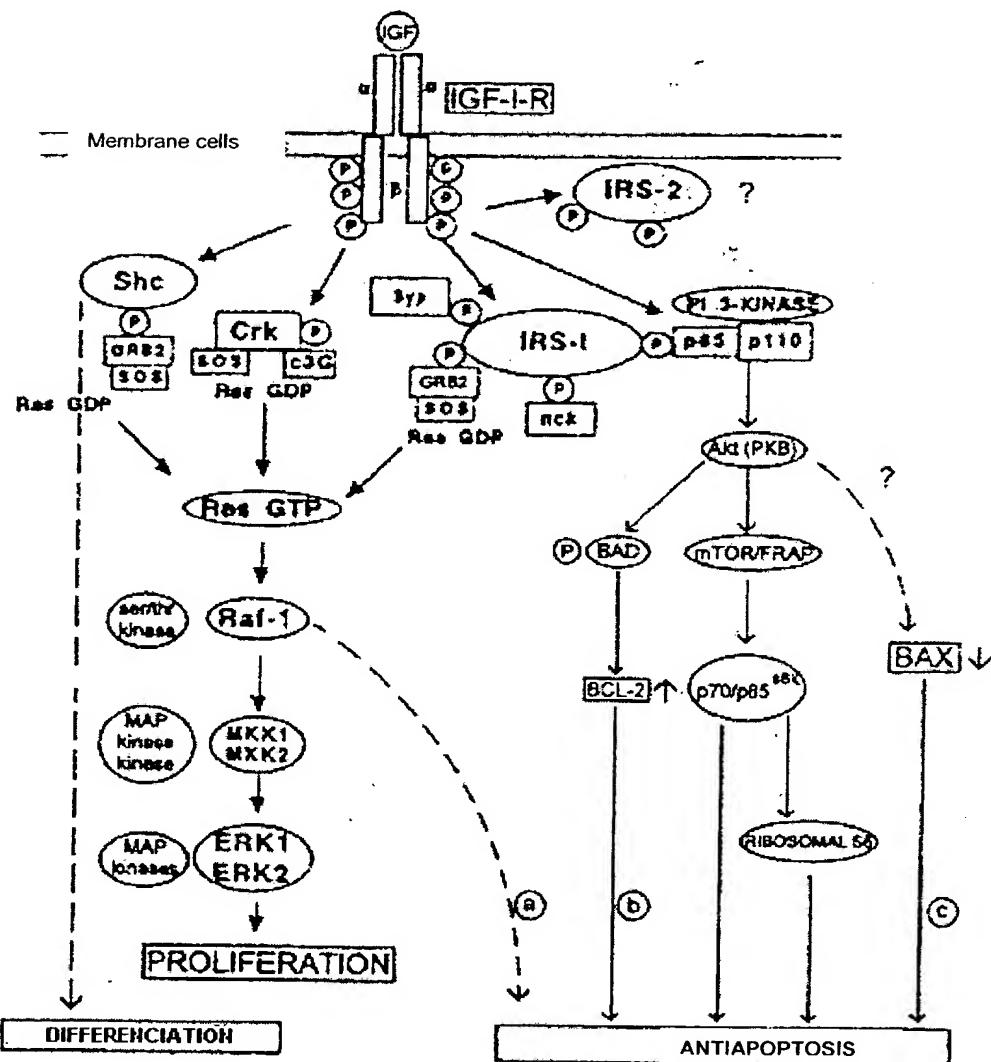


FIGURE 2

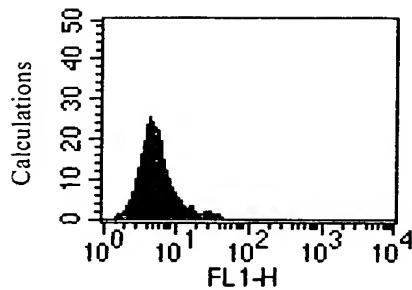


FIGURE 3A

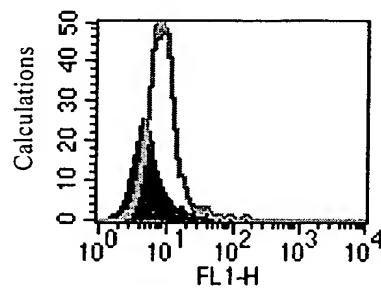


FIGURE 3B

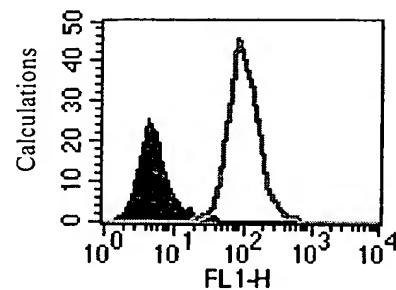
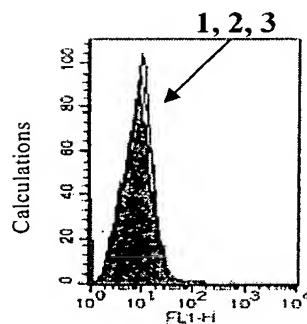
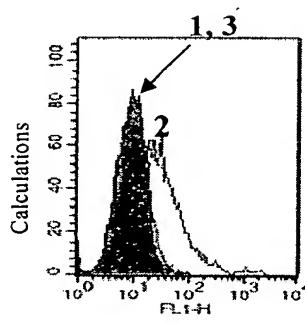


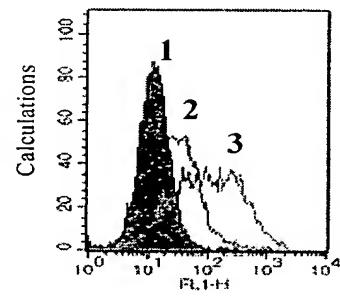
FIGURE 3C



Nontransfected cells



IGF-IR+ cells



IR+ cells

FIGURE 4A

FIGURE 4B

FIGURE 4C

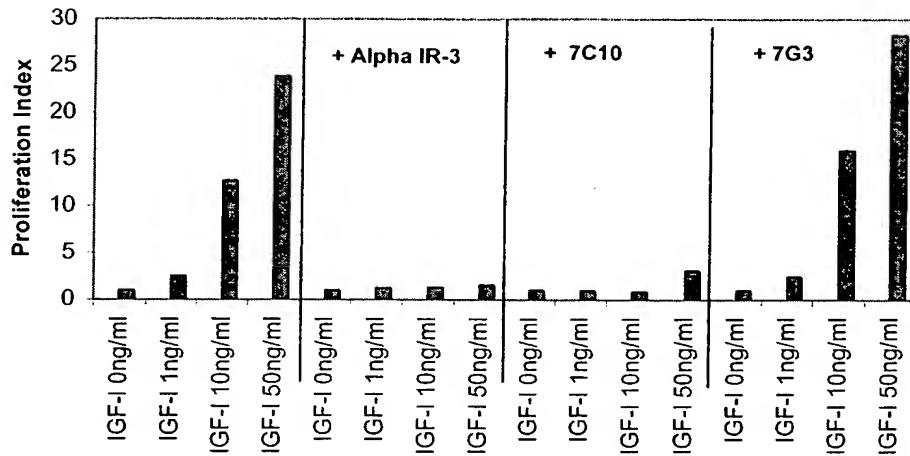


FIGURE 5

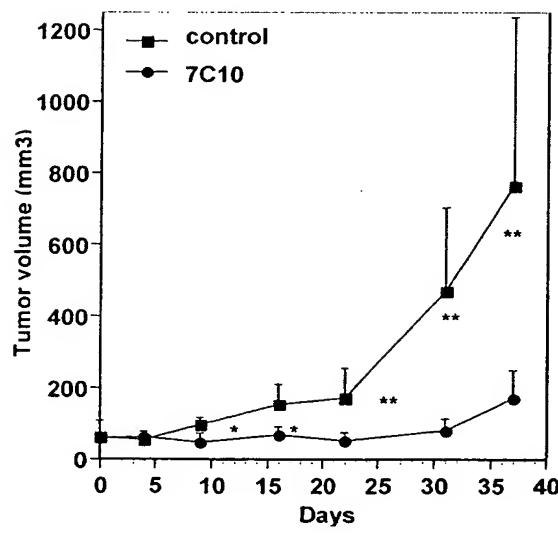


FIGURE 6A

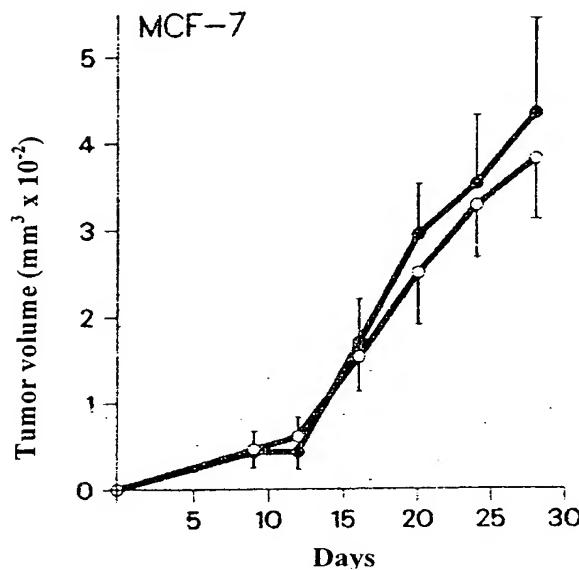


FIGURE 6B

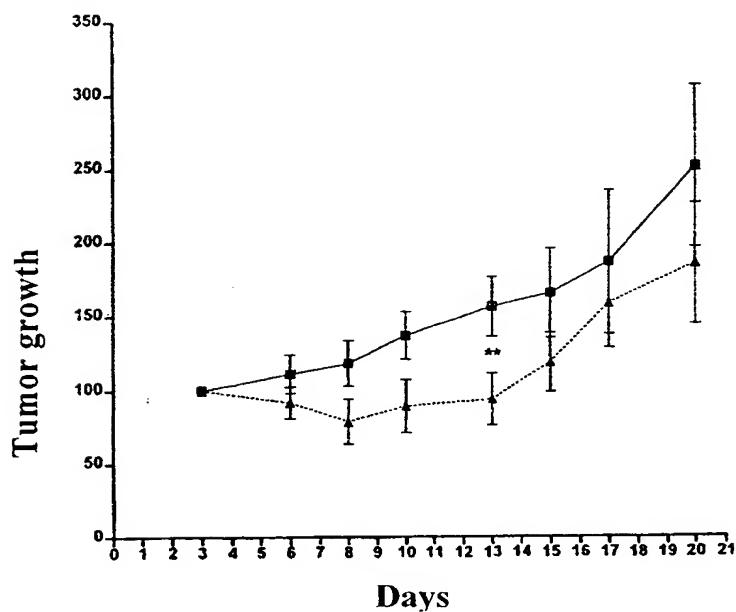


FIGURE 6C

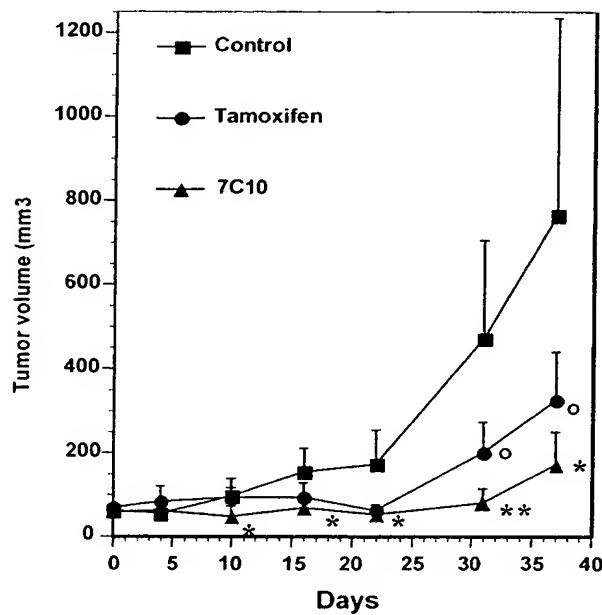


FIGURE 7

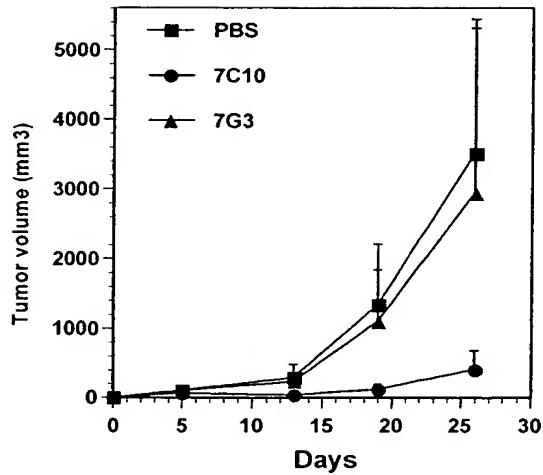


FIGURE 8A

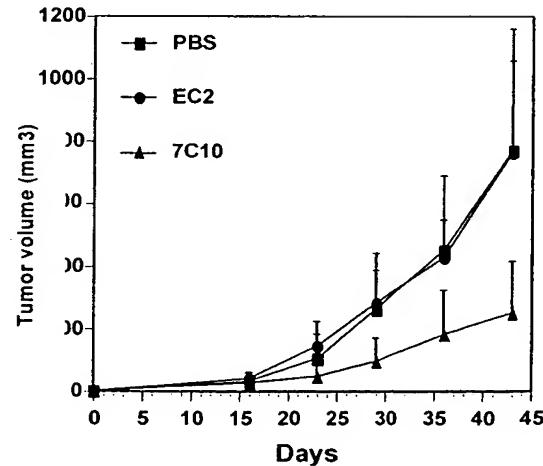


FIGURE 8B

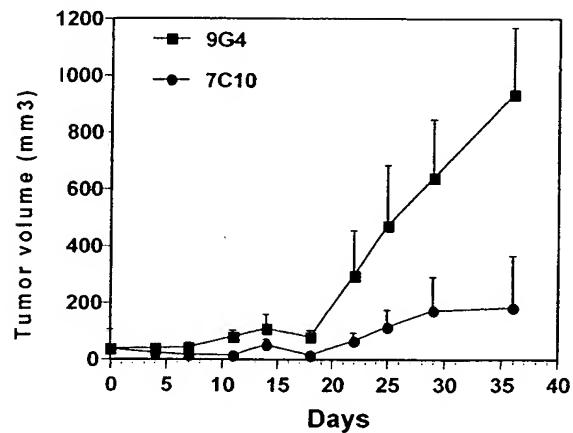


FIGURE 8C

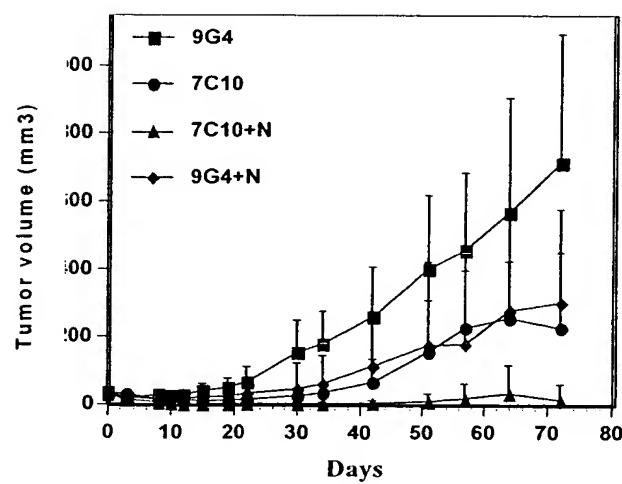


FIGURE 9

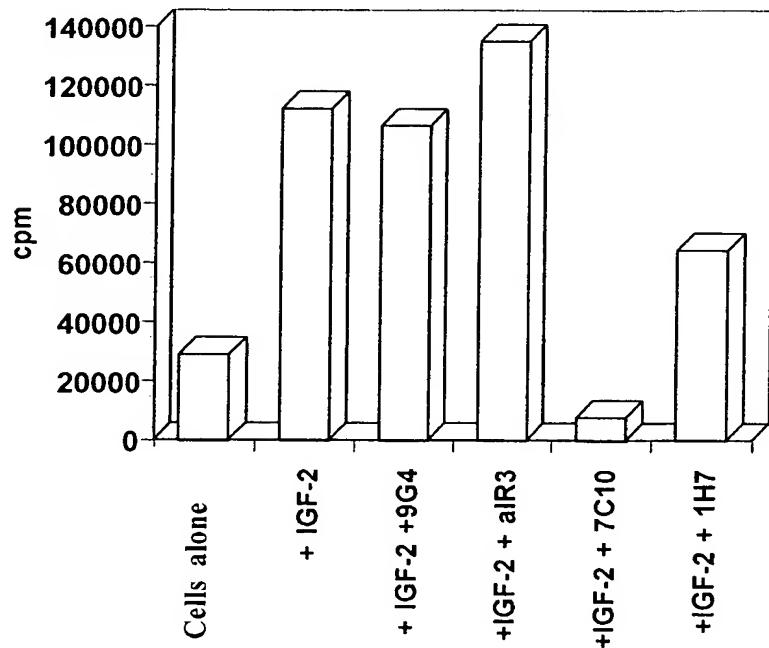


FIGURE 10

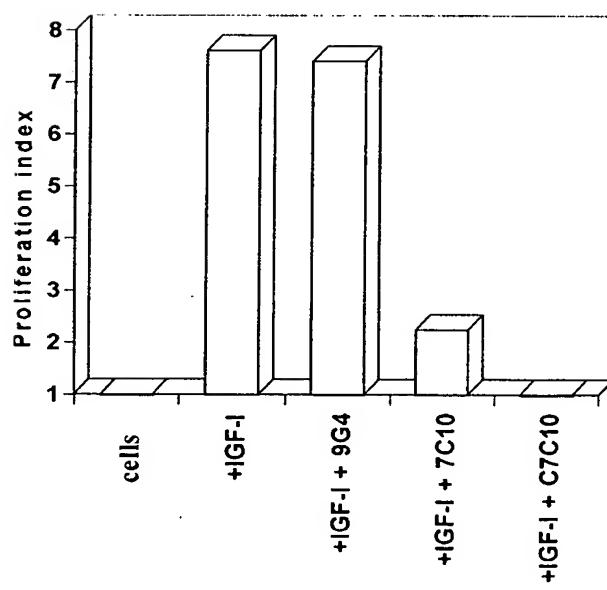


FIGURE 11

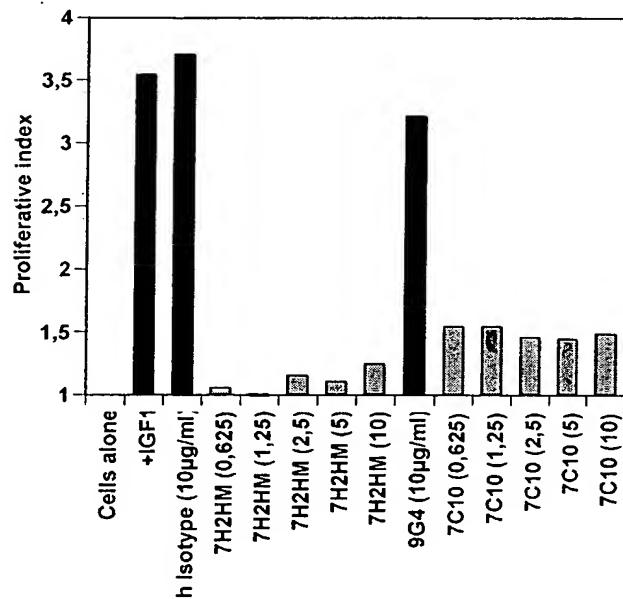


FIGURE 12

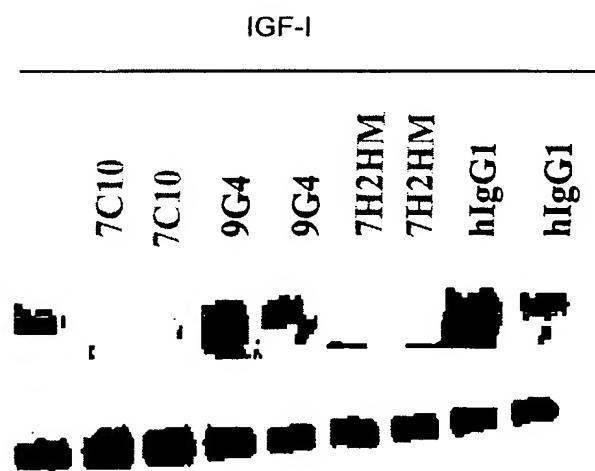


FIGURE 13

ATGAAGTTGCCTGTTAGGCTGTTGGTGTGATGTTCTGGATTCCTGCTTCCAGAAGTGAT
 1 -----+-----+-----+-----+-----+-----+-----+-----+-----+ 60
 TACTTCAACGGACAATCCGACAACCACGACTACAAGACCTAAGGACGAAGGTCTTCACTA
 ATGAAGTTGCCTGTTAGGCTGTTGGTGTGATGTTCTGGTGTGCT
oligo MKV-1 L M F W I P A S R S D -
 3' end *leader peptide*
 GTTTTGATGACCCAAATTCCACTCTCCCTGCCTGTCAGTCTGGAGATCAAGCCTCCATC
 61 -----+-----+-----+-----+-----+-----+-----+-----+ 120
 CAAAACACTGGGTTAAGGTGAGAGGGACGGACAGTCAGAACCTCTAGTTGGAGGTAG
 V L M T Q I P L S L P V S L G D Q A S I -
 TCTTGCAGATCTAGTCAGAGCATTGTACATAGTAATGGAAACACCTATTACAATGGTAC
 121 -----+-----+-----+-----+-----+-----+-----+-----+ 180
 AGAACGTCTAGATCAGTCTCGTAACATGTATCATTACCTTGTGGATAATGTTACCATG
 S C R S S Q S I V H S N G N T Y L Q W Y -
 CDR 1
 CTGCAGAAACCAGGTCAGTCTCAAAGCTCCTGATCTACAAAGTTCCAACCGACTTTAT
 181 -----+-----+-----+-----+-----+-----+-----+-----+ 240
 GACGTCTTGGTCCAGTCAGAGGTTTCGAGGACTAGATGTTCAAAGGTGGCTGAAATA
 L Q K P G Q S P K L L I Y K V S N R L Y -
 CDR 2
 GGGGTCCCAGACAGGTTCAGTGGCAGTGGATCAGGGACAGATTCACACTCAAGATCAGC
 241 -----+-----+-----+-----+-----+-----+-----+-----+ 300
 CCCCAGGGTCTGTCCAAGTCACCGTCACCTAGTCCCTGTCTAAAGTGTGAGTTCTAGTCG
 G V P D R F S G S G S G T D F T L K I S -
 AGCGTGGAGGCTGAGGATCTGGGAGTTATTACTGCTTCAAGGTTCACATGTTCCGTGG
 301 -----+-----+-----+-----+-----+-----+-----+-----+ 360
 TCGCACCTCCGACTCCTAGACCCCTAAATAATGACGAAAGTCCAAGTGTACAAGGCACC
 S V E A E D L G V Y Y C F Q G S H V P W -
 CDR 3
 GG
 ACGTTCGGTGGAGGCACCAAGCTGGAAATCAAACGGGCTGATGCTGCACCAACTGTATCC
 361 -----+-----+-----+-----+-----+-----+-----+-----+ 420
 TGCAAGCCACCTCCGTGGTTGACCTTAGTTGCCGACTACGACGTGGTTGACATAGG
 T F G G G T K L E I K
 MKC oligo
 TAGAAGGGTGGTAGGTCA
 ATCTTCCCACCATCCAGT
 421 -----+----- 438
 TAGAAGGGTGGTAGGTCA

FIGURE 14

1 ATGATGGTGTAAAGTCTCTGTACCTCTTGACAGCCATTCTGGTATCCTGTCTGATGTA 60
 1-----+-----+-----+-----+-----+-----+
 1 TACTACCACAATTCAAGAACATGGACAACTGTCGGTAAGGACCATAGGACAGACTACAT
MHV-12 ATGATGGTGTAAAGTCTCTGTACCT
MHV-8 ATGAGAGTGCTGATTCTTTGTG

L L T A I P G I L S D V -
 3' end leader peptide

61 CAGCTTCAGGAGTCAGGACCTGGCCTCGTAAACCTTCTCAGTCTCTGTCTCACCTGC 120
 61-----+-----+-----+-----+-----+-----+
 61 GTCGAAGTCCTCAGTCCTGGACCGGAGCACTTGGAAAGAGTCAGAGACAGAGAGTGGACG

Q L Q E S G P G L V K P S Q S L S L T C -
 121 TCTGTCACCGGCTACTCCATACCGGTGGTTATTATGGAACCTGGATCCGGCAGTTCCA 180
 121-----+-----+-----+-----+-----+-----+
 121 AGACAGTGGCCGATGAGGTAGTGGCCACCAATAACCTTGACCTAGGCCGTCAAAGGT

S V T G Y S I T G G Y L W N W I R Q F P -
 181 CDR 1
 181 GAAACAAACTGGAGTGGATGGCTACATAAGCTACGACGGTACCAAACTACAAACCA 240
 181-----+-----+-----+-----+-----+-----+
 181 CCTTTGTTGACCTCACCTACCCGATGTATTGATGCTGCCATGGTTATTGATGTTGGT

G N K L E W M G Y I S Y D G T N N Y K P -
 241 CDR 2
 241 TCTCTCAAAGATCGAATCTCCATCACTCGTGACACATCTAAGAACAGTTTCCTGAAG 300
 241-----+-----+-----+-----+-----+-----+
 241 AGAGAGTTCTAGCTTAGAGGTAGTGAGCACTGTGTAGATTCTGGTCAAAAGGACTTC

S L K D R I S I T R D T S K N Q F F L K -
 301 TTGAATTCTGTGACTAATGAAGACACAGCTACATATTACTGTGCAAGATAACGGTAGGGTC 360
 301-----+-----+-----+-----+-----+-----+
 301 AACTTAAGACACTGATTACTCTGTGTCATGTATAATGACACGTTCTATGCCATCCCAG

L N S V T N E D T A T Y Y C A R Y G R V -
 361 CDR 3
 361 GGG
 361 TTCTTTGACTACTGGGCCAAGGCACCACTCTCACAGTCTCCTCAGCCAAAACGACACCC 420
 361-----+-----+-----+-----+-----+-----+
 361 AAGAAACTGATGACCCCGGTTCCGTGGTGAGAGTGTCAAGAGGAGTCGGTTTGCTGTGGG

F F D Y W G Q G T T L T V S S
 421 oligo MHC-1
 421 GGTAGACAGATAGGTGAC
 421 CCATCTGTCTATCCACTG
 421 ----- 438
 421 GGTAGACAGATAGGTGAC

FIGURE 15

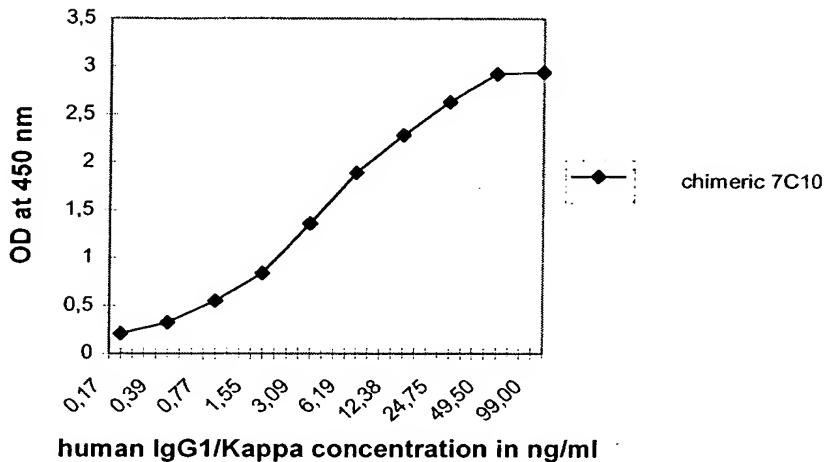


FIGURE 16

3 7 *CDR 1*

7C10 VL mouse	DVLMTQ <u>I</u> PLSLPVSLGDQASISC	RSSQSIVHSNGNTYLO
DRB1-4.3T..... E
C94-5B11' CLT..... E
Kabat sgII mouse	<u>V</u> ... <u>T</u> L E

CDR 2

7C10 VL mouse	WYLQKPGQSPKLLIY	KVSNRLY GVPDRFSGSGSGTDFTL
DRB1-4.3 FS
C94-5B11' CL FS
Kabat sgII mouse FS

77 *CDR 3*

7C10 VL mouse	KISSVEAEDLGVYYC	FQGSHVPWT FGGGTKLEIK
DRB1-4.3	...R..... F ...S...D...
C94-5B11' CL	...R.....
Kabat sgII mouse	... <u>R</u> T ... Y

FIGURE 17

CDR 1
 7C10 VL mouse DVLMTQIPLSLPVSLGDQASISC RSSQSIVHSNGNTYLO
 GM607 .IV...S.....TP.EP..... .LL....YN..D
 DPK15/A19 .IV...S.....TP.EP..... .LL....YN..D
 Kabat sgII hu .IV...S.....TP.EP..... .LL..D.XX..X

CDR 2
 7C10 VL mouse WYLQKPGQSPKLLIY KVSNRLY GVPDRFSGSGSGTDFTLK
 GM607Q.... LG...AS ..
 DPK15/A19Q.... LG...AS ..
 Kabat sgII huQ.... L....AS ..

CDR 3
 7C10 VL mouse ISSVEAEDLGVYYC FQGSHVPWT FGGGTKLEIK
 GM607 ..R.....V.... M.ALQT.Q. ..Q...V...
 DPK15/A19 ..R.....V.... M.ALQT.
 Kabat sgII hu ..R.....V.... M.ALQX.R. ..Q...V...

FIGURE 18

CDR 1
 7C10 VL mouse DVLMTQIPLSLPVSLGDQASISC RSSQSIVHSNGNTYLO
 GM 607 .IV...S.....TP.EP..... .LL....YN..D
 7C10 VL Humanized 1 .V...S.....TP.EP..... ..
 7C10 VL Humanized 2 .IV...S.....TP.EP..... ..

CDR 2
 7C10 VL mouse WYLQKPGQSPKLLIY KVSNRLY GVPDRFSGSGSGTDFTL
 GM 607Q.... LG...AS ..
 7C10 VL Humanized 1Q.... ..
 7C10 VL Humanized 2Q.... ..

CDR 3
 7C10 VL mouse KISSVEAEDLGVYYC FQGSHVPWT FGGGTKLEIK
 GM 607 ...R.....V.... M.ALQT.Q. ..Q...V...
 7C10 VL Humanized 1 ...R.....V....Q...V...
 7C10 VL Humanized 2 ...R.....V....Q...V...

FIGURE 19

MluI

1 GTCAGAACGCGTGCCGCCACCATGAAGTTGCCTGTTAGGCTGTTGGTGCATGTTCTGG
 1 CAGTCTGCGCACGGCGGTGGTACTTCAACGGACAATCCGACAACCACGACTACAAGACC 60

2 M K L P V R L L V L M F W -
 Peptide leader

61 TTTCCTGCTTCCAGCAGTGTAGTTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACC
 61 AAAGGACGAAGGTCGTCACTACAAACACTACTGAGTCAGAGGTGAGAGGGACGGCAGTGG 120

2 F P A S S S D V V M T Q S P L S L P V T -

121 CCTGGAGAGCCGGCCTCCATCTCCTGCAGGTCTAGTCAGAGCATTGTACATAGTAATGGA
 121 GGACCTCTGGCCGGAGGTAGAGGACGTCCAGATCAGTCTCGTAACATGTATCATTACCT 180

CDR 1
 P G E P A S I S C R S S Q S I V H S N G -
 KpnI

181 AACACCTATTGCAATGGTACCTGCAGAACGCCAGGGCAGTCTCCACAGCTCCTGATCTAT
 181 TTGTGGATAAACGTTACCATGGACGTCTCGGTCCCGTCAGAGGTGTCAGGACTAGATA 240

N T Y L Q W Y L Q K P G Q S P Q L L I Y -

241 AAAGTTTCTAATCGGCTTATGGGGTCCCTGACAGGTTCAGTGGCAGTGGATCAGGCACA
 241 TTTCAAAGATTAGCCGAAATACCCAGGGACTGTCCAAGTCACCGTCACCTAGTCCGTGT 300

CDR 2
 K V S N R L Y G V P D R F S G S G S G T -

301 GATTTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTTGGGTTTATTACTGCTTT
 301 CTAAAATGTGACTTTAGTCGTCTACCTCCGACTCCTACAACCCCAAATAATGACGAAA 360

D F T L K I S R V E A E D V G V Y Y C F -

361 CAAGGTTCACATGTTCCGTGGACGTTGGCCAAGGGACCAAGGTGGAAATCAAACGTGAG
 361 GTTCCAAGTGTACAAGGCACCTGCAAGCCGGTCCCTGGTCCACCTTAGTTGCACTC 420

CDR 3
 Q G S H V P W T F G Q G T K V E I K

BamHI

421 TGGAATCCTCTGCG 433
 421 ACCTAGGAGACGC

FIGURE 20

MluI

1 GTCAGAACGCGTGCCGCCACCATGAAGTTGCCTGTTAGGCTGTTGGTGCTGATGTTCTGG
 1-----+-----+-----+-----+-----+-----+-----+ 60
 CAGTCTGCGCACGGCGGTGGTACTTCAACGGACAATCCGACAACCACGACTACAAGACC

2 M K L P V R L L V L M F W -
 Leader peptide
 61 TTTCCTGTTCCAGCAGTGATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACC
 61-----+-----+-----+-----+-----+-----+-----+ 120
 AAAGGACGAAGGTCGTCACTACAACACTACTGAGTCAGAGGTGAGAGGGACGGGCAGTGG
 2 F P A S S S D I V M T Q S P L S L P V T -
 CCTGGAGAGCCGGCCTCCATCTCCTGCAGGTCTAGTCAGAGCATTGTACATAGTAATGGA
 121-----+-----+-----+-----+-----+-----+-----+ 180
 GGACCTCTGGCCGGAGGTAGAGGACGTCCAGATCAGTCTCGTAACATGTATCATTACCT
 CDR 1
 P G E P A S I S C R S S Q S I V H S N G -
 KpnI
 181 AACACCTATTCGAATGGTACCTGCAGAACGCCAGGGCAGTCTCCACAGCTCCTGATCTAT
 181-----+-----+-----+-----+-----+-----+-----+ 240
 TTGTGGATAAACGTTACCATGGACGTCTCGGTCCCGTCAGAGGTGTCGAGGACTAGATA
 N T Y L Q W Y L Q K P G Q S P Q L L I Y -
 AAAGTTTCTAATCGGTTATGGGGTCCCTGACAGGTTCAAGGGCAGTGGATCAGGCACA
 241-----+-----+-----+-----+-----+-----+-----+ 300
 TTTCAAAGATTAGCCGAAATACCCAGGGACTGTCCAAGTCACCGTCACCTAGTCGTG
 CDR 2
 K V S N R L Y G V P D R F S G S G S G T -
 GATTTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTTGGGTTATTACTGCTTT
 301-----+-----+-----+-----+-----+-----+-----+ 360
 CTAAAATGTGACTTTAGTCGTCTCACCTCCGACTCCTACAACCCCAAATAATGACGAAA
 D F T L K I S R V E A E D V G V Y Y C F -
 CAAGGTTCACATGTTCCGTGGACGTTCCGCCAACGGACCAAGGTGAAATCAAACGTGAG
 361-----+-----+-----+-----+-----+-----+-----+ 420
 GTTCCAAGTGTACAAGGCACCTGCAAGCCGGTCCCTGGTCCACCTTAGTTGCACTC
 CDR 3
 Q G S H V P W T F G Q G T K V E I K
 BamHI
 421 TGGATCCTCTGCG 433
 ACCTAGGAGACGC

FIGURE 21

17 27 **CDR 1**
7C10 VH DVQLQESGPGLVKPSQSLSLTCSVTGYSIT **GGYLWN** WIRQ
AN03' CL **S..Y..** ..
 Kabat sgI(A) E.....S.....T.....D... **S..WN.** ...

CDR 2
7C10 VH FPGNKLEWMG **YISYDGTNNYKPSLKD** RISITRDTSKNQFFL
AN03' CL **N...N...N...N** ..
 Kabat sgI(A) **S.STY.N...S** Y..

84 **CDR 3**
7C10 VH KLNSVTNEDTATYYCAR **YGRV-FFDY** WGQGTTLTVSS
AN03' CL T..... **E.YGY..** ..
 Kabat sgI(A) Q.....T..... **G.YGYG..** .. V...

FIGURE 22

Rch 1 30 **CDR 1 Rch 2**
7C10 VH mouse DVQLQESGPGLVKPSQSLSLTCSVTGYSIT **GGYLWN** WIRQ
human Kabat sgII Q.....T.....T.S.G.VS **SYWS..** ...
human VH FUR1' CL Q.....ET.....T.S....S **S..Y.S** ...
human Germline Q.....ET.....T.S....S **S..Y.S** ...

Rch 2 48 **CDR 2** 67 71 **Rch 3**
7C10 VH mouse FPGNKLEWMG **YISYDGTNNYKPSLKD** RISITRDTSKNQFFL
human Kabat sgII P..KG...I. **R.Y.S.STX.N...S** .VT.SV.....S.
human VH FUR1' CL P..KG...I. **SMFHS.SSY.N...S** .VT.SV.....S.
human Germ-line P..KG...I. **S.YHS.STY.N...S** .VT.SV.....S.

Rch 3 **CDR 3** **Rch 4**
7C10 VH mouse KLNSVTNEDTATYYCAR **YGRVFFDY** WGQGTTLTVSS
human Kabat sgII ..S...AA...V..... **ELPGGYDV**LV....
human VH FUR1' CL Q.R...AA...V..... **GRYCSSTSCNWFDP**LV....
human Germline ..S...AA...V.....

FIGURE 23

		30	CDR 1	48	
7C10 VH mouse	DVQLQESGPGLVKPSQSLSLTCVTGYSIT	<u>GGYLWN</u>	WIRQFPGNKLEWMG		
human germline	Q.....	ET.....	T.S.....	<u>S</u> S..Y.G	P..KG... <u>I</u>
VH Humanized 1	Q.....	ET.....	T.S.....	P..KG.....
VH Humanized 2	Q.....	ET.....	T.S.....	P..KG... <u>I</u>
VH Humanized 3	Q.....	ET.....	T.S.....	<u>S</u>	P..KG... <u>I</u>
		CDR 2	67	71	
7C10 VH mouse	<u>YISYDGTNNYKPSLKD</u>	RISIT	<u>RDT</u>	TSKNQFFLKLNSVTNEDTATYYCAR	
human germline	S.FHS.SSY.N....S	<u>VT</u> .	<u>SV</u>	S...S...AA...V.....
VH Humanized 1	T.S.....	S...S...AA...V.....
VH Humanized 2	<u>VT</u> .	S.....	S...S...AA...V.....
VH Humanized 3	<u>VT</u> .	<u>SV</u>	S...S...AA...V.....
		CDR 3			
7C10 VH mouse	<u>YGRVFFDY</u>	WGQGTTLT	VSS		
human germline	LV.....		
VH Humanized 1	LV.....		
VH Humanized 2	LV.....		
VH Humanized 3	LV.....		

FIGURE 24

MluI

1 |
 GTCAGAACGCGTGCCGCCACCATGAAAGTGGTGGAGTCTGTTGTACCTCTTGACAGCCATT
 1-----+-----+-----+-----+-----+-----+ 60
 CAGTCTGCGCACGGCGGTGGTACTTCAACACTCAGACAAACATGGAGAACTGTCGGTAA

 M K V L S L L Y L L T A I -
 Leader peptide
 CCTGGTATCCTGTCAGGTGCAGCTTCAGGAGTCGGGCCAGGACTGGTGAAGCCTCG
 61 -----+-----+-----+-----+-----+-----+ 120
 GGACCATAGGACAGAGTCCACGTCGAAGTCCTCAGCCGGTCCTGACCACCTCGGAAGC

 P G I L S Q V Q L Q E S G P G L V K P S -

 GAGACCTGTCCCTCACCTGCACTGTCTGGTTACTCCATACCGGTGGTTATTATGG
 121 -----+-----+-----+-----+-----+-----+ 180
 CTCTGGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTGGCCACCAATAATACC
 30 CDR 1
 E T L S L T C T V S G Y S I T G G Y L W -

 AACTGGATAACGGCAGCCCCAGGGAAAGGGACTGGAGTGGATGGGTATATCAGCTACGAC
 181 -----+-----+-----+-----+-----+-----+ 240
 TTGACCTATGCCGTCGGGGTCCCTCCCTGACCTCACCTACCCATATAGTCGATGCTG
 48
 N W I R Q P P G K G L E W M G Y I S Y D -
 KpnI
 |
 GGTACCAATAACTACAAACCTCCCTCAAGGATCGAATCACCATATCACGTGACACGTCC
 241 -----+-----+-----+-----+-----+-----+ 300
 CCATGGTTATTGATGTTGGGAGGGAGTCCTAGCTAGTGGTATAGTCGACTGTGCAGG
 CDR 2 67 71
 G T N N Y K P S L K D R I T I S R D T S -

 AAGAACCAAGTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACTGCAGTGTATTAC
 301 -----+-----+-----+-----+-----+-----+ 360
 TTCTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCGTGACGTCACATAATG

 K N Q F S L K L S S V T A A D T A V Y Y -

 TGTGCGAGATAACGGTAGGGCTTCTTGTACTACTGGGCCAGGGAACCCCTGGTCACCGTC
 361 -----+-----+-----+-----+-----+-----+ 420
 ACACGCTCTATGCCATCCCAGAAGAAACTGATGACCCCGTCCCTGGGACCAAGTGGCAG
 CDR 3
 C A R Y G R V F F D Y W G Q G T L V T V -

 BamHI
 |
 TCCTCAGGTGAGTGGATCCTCTGCG
 421 -----+-----+-----+-----+-----+-----+ 445
 AGGAGTCCACTCACCTAGGAGACGC

 S S -

FIGURE 25

MluI

1 GTCAGAACGCGTGCCGCCACCATGAAAGTGGTGGAGTCTGTTGTACCTCTTGACAGCCATT
 1 CAGTCTGCGCACGGCGGTGGTACTTCACAACTCAGACAAACATGGAGAACTGTCGGTAA 60

M K V L S L L Y L L T A I -
 Leader peptide

61 CCTGGTATCCTGCTCAGGGCAGCTTCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCG
 61 GGACCATAGGACAGAGTCCACGTCGAAGTCCTCAGCCCAGGCTGACCACTTCGGAAGC 120

P G I L S Q V Q L Q E S G P G L V K P S -
 Leader peptide

121 GAGACCTGTCCTCACCTGCACTGTCTGGTTACTCCATCACGGTGGTTATTATGG
 121 CTCTGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTCGCCACCAATAATACC 180

30 CDR 1
 E T L S L T C T V S G Y S I T G G Y L W -
 Leader peptide

181 AACTGGATAACGGCAGCCCCAGGGAGGGACTGGAGTGGATCGGGTATATCAGCTACGAC
 181 TTGACCTATGCCGTGGGGTCCCTCCCTGACCTCACCTAGCCATATAGTCGATGCTG 240

48
 N W I R Q P P G K G L E W I G Y I S Y D -
 Leader peptide

KpnI

241 GGTACCAATAACTACAAACCTCCCTCAAGGATCGAGTCACCATATCACGTGACACGTCC
 241 CCATGGTTATTGATGTTGGAGGGAGTCCTAGCTCAGTGGTATAGTGCAGTGTGCAGG 300

CDR 2 67 71
 G T N N Y K P S L K D R V T I S R D T S -
 Leader peptide

301 AAGAACCAAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACTGCAGTGTATTAC
 301 TTCTTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCGTGACGTCACATAATG 360

K N Q F S L K L S S V T A A D T A V Y Y -
 Leader peptide

361 TGTGCGAGATAACGGTAGGGCTTCTTGTACTACTGGGCCAGGGAACCTGGTCACCGTC
 361 ACACGCTCTATGCCATCCCAGAAGAAACTGATGACCCGGTCCCTGGGACCAAGTGGCAG 420

CDR 3
 C A R Y G R V F F D Y W G Q G T L V T V -
 Leader peptide

BamHI

421 TCCTCAGGTGAGTGGATCCTCTGCG
 421 AGGAGTCCACTCACCTAGGAGACGC 445

S S -
 Leader peptide

FIGURE 26

MluI

1 GTCAGAACGCGTGCCGCCACCATGAAAGTGTGAGTCTGTTGTACCTCTTGACAGCCATT
 1 CAGTCTGCGCACGGCGGTGGTACTTCACAACTCAGACAACTGGAGAACTGTCGGTAA 60

2 Leader peptide

61 CCTGGTATCCTGTCTCAGGTGCAGCTTCAGGAGTCGGGCCAGGACTGGTGAAGCCTCG
 61 GGACCATAGGACAGAGTCCACGTCGAAGTCCTCAGCCGGTCCTGACCACCTCGGAAGC 120

3 P G I L S Q V Q L Q E S G P G L V K P S -

4 GAGACCTGTCCCTCACCTGCACTGTCCTGGTTACTCCATCAGCGTGGTTATTATGG
 121 CTCTGGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTCGCCACCAATAATACC 180

5 E T L S L T C T V S G Y S I S G G Y L W -

6 AACTGGATAACGGCAGCCCCAGGGAAAGGGACTGGAGTGGATCGGGTATATCAGCTACGAC
 181 TTGACCTATGCCGTCGGGGTCCCTCCCTGACCTCACCTAGCCCATAAGTCGATGCTG 240

7 N W I R Q P P G K G L E W I G Y I S Y D -

8 KpnI

9 GGTACCAATAACTACAAACCTCCCTCAAGGATCGAGTCACCATATCAGTGGACACGTCC
 241 CCATGGTTATTGATGTTGGGAGGGAGTCCTAGCTCAGTGGTATAGTCACCTGTGCAGG 300

10 CDR 2 G T N N Y K P S L K D R V T I S V D T S -

11 AAGAACCAAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACTGCAGTGTATTAC
 301 TTCTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCGTGACGTCACATAATG 360

12 K N Q F S L K L S S V T A A D T A V Y Y -

13 TGTGCGAGATAACGGTAGGGTCTCTTGACTACTGGGCCAGGGAACCCCTGGTCACCGTC
 361 ACACGCTCTATGCCATCCCAGAAGAAACTGATGACCCCGTCCCTGGGACAGTGGCAG 420

14 CDR 3 C A R Y G R V F F D Y W G Q G T L V T V -

15 BamHI

16 TCCTCAGGTGAGTGGATCCTCTGCG
 421 AGGAGTCCACTCACCTAGGAGACGC 445

17 S S

FIGURE 27

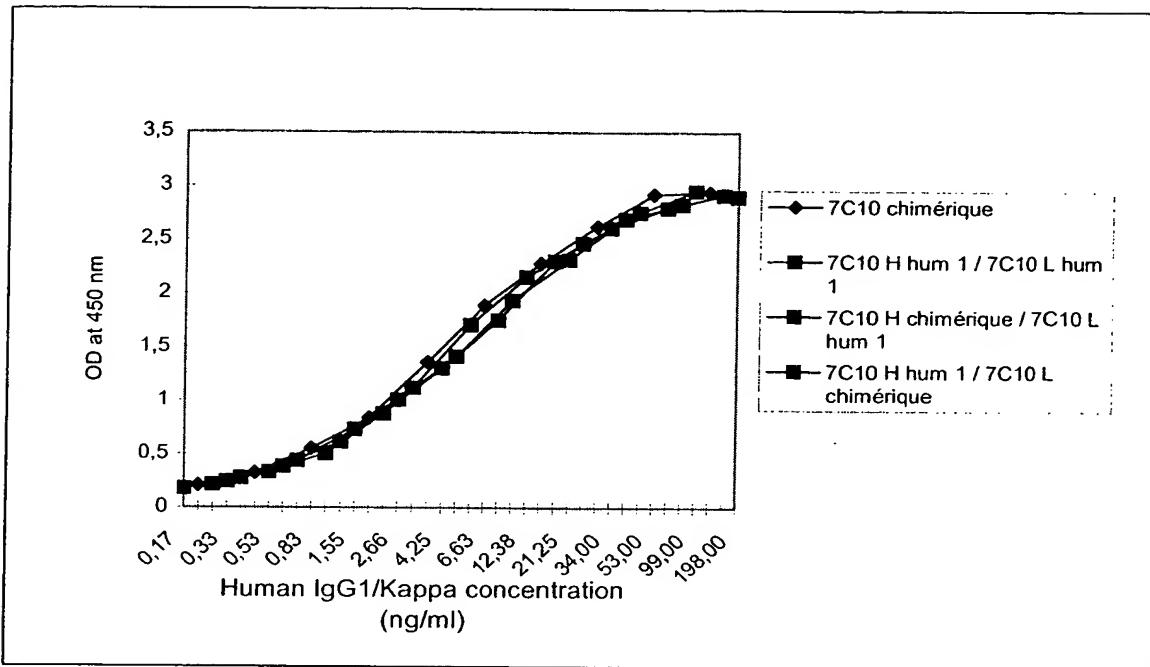


FIGURE 28

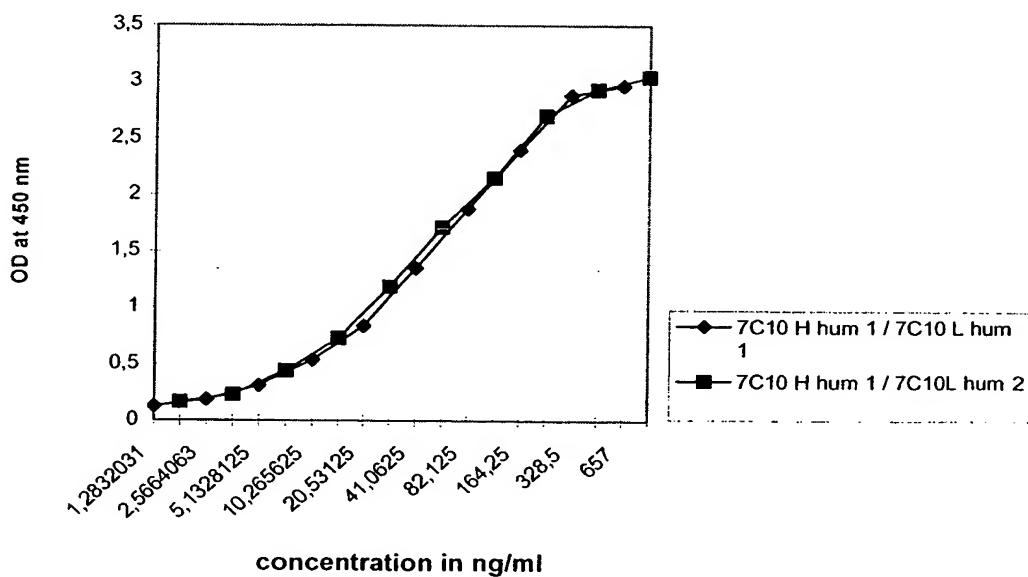


FIGURE 29

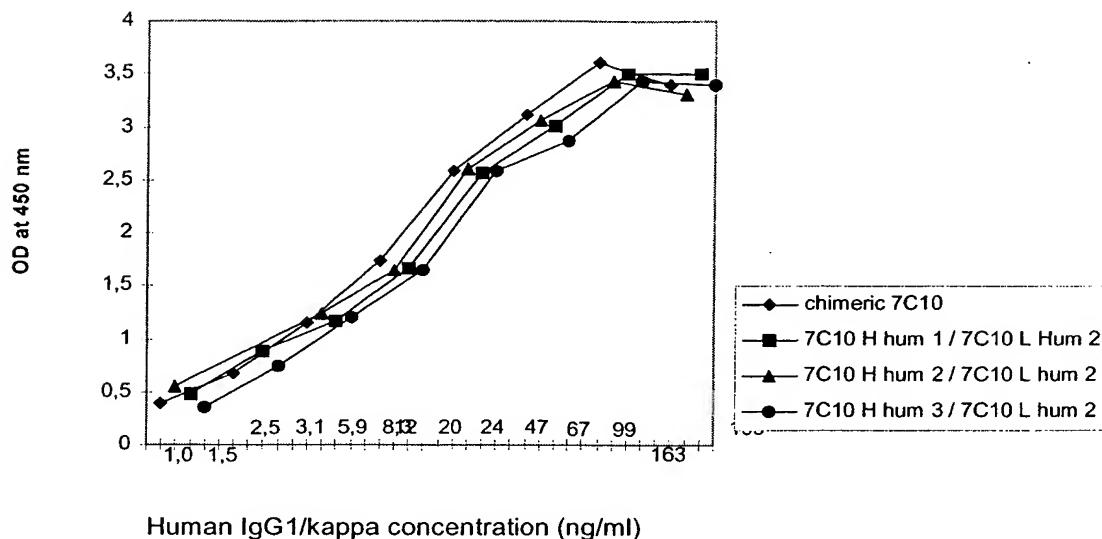


FIGURE 30

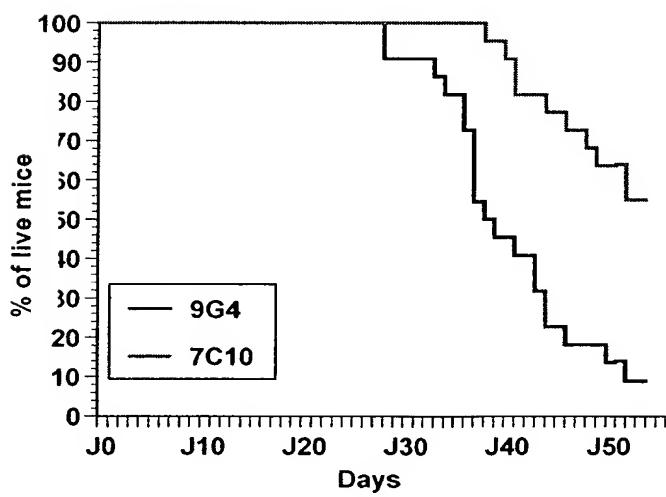


FIGURE 31

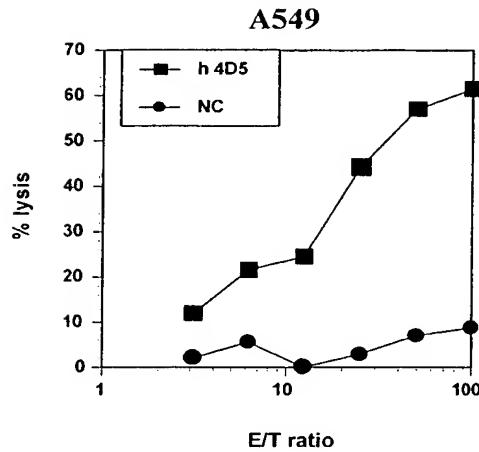


FIGURE 32A

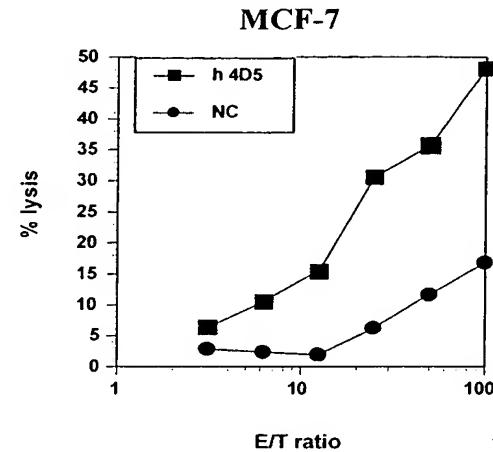


FIGURE 32B

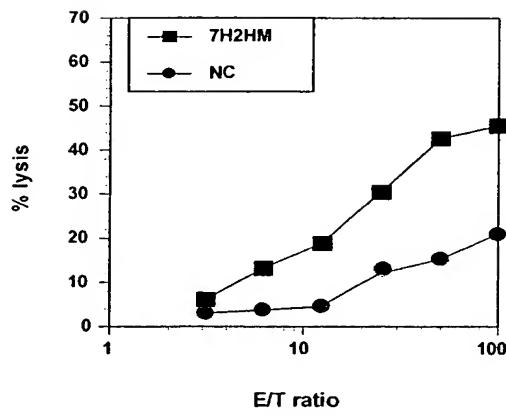


FIGURE 32C

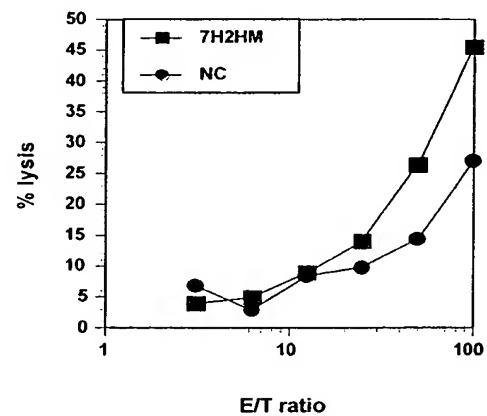
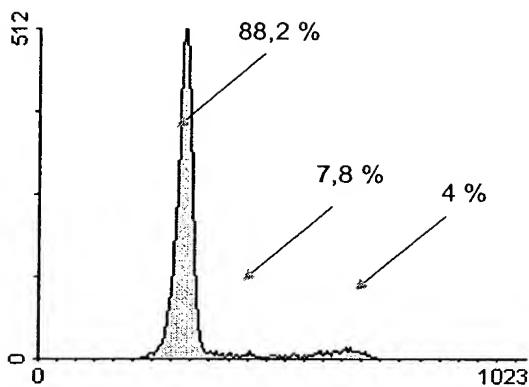


FIGURE 32D

- IGF1



+ IGF1 (50 ng/ml)

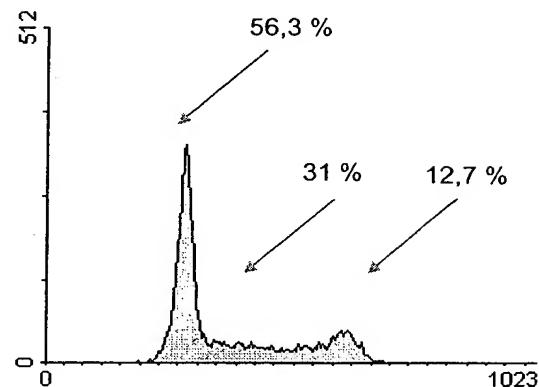


FIGURE 33A

FIGURE 33B

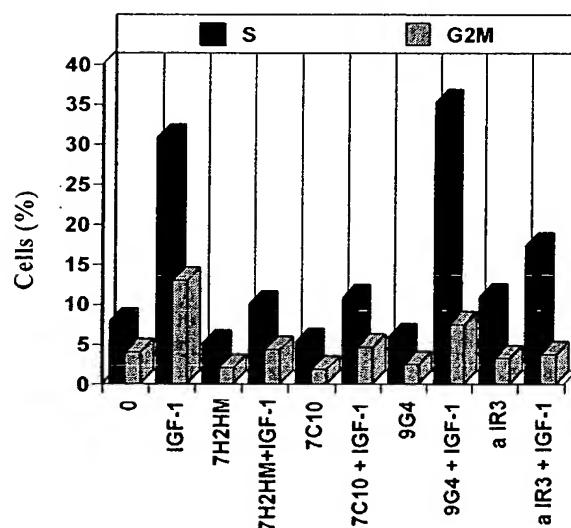


FIGURE 33C

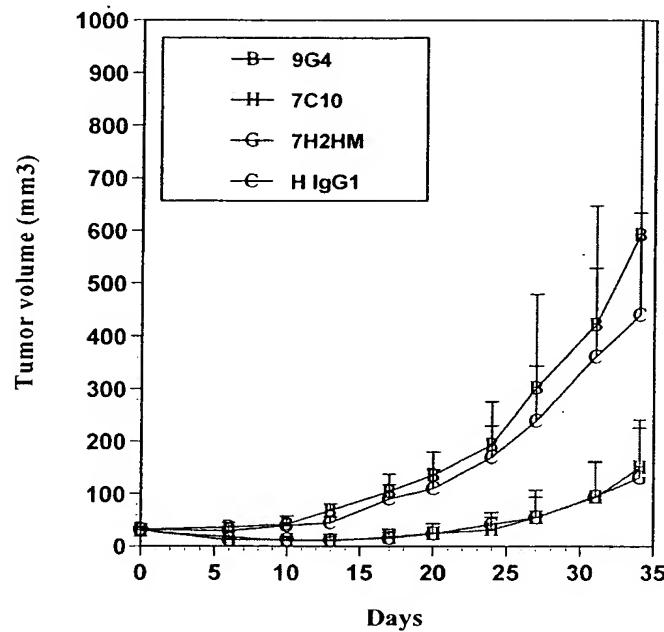


FIGURE 34A

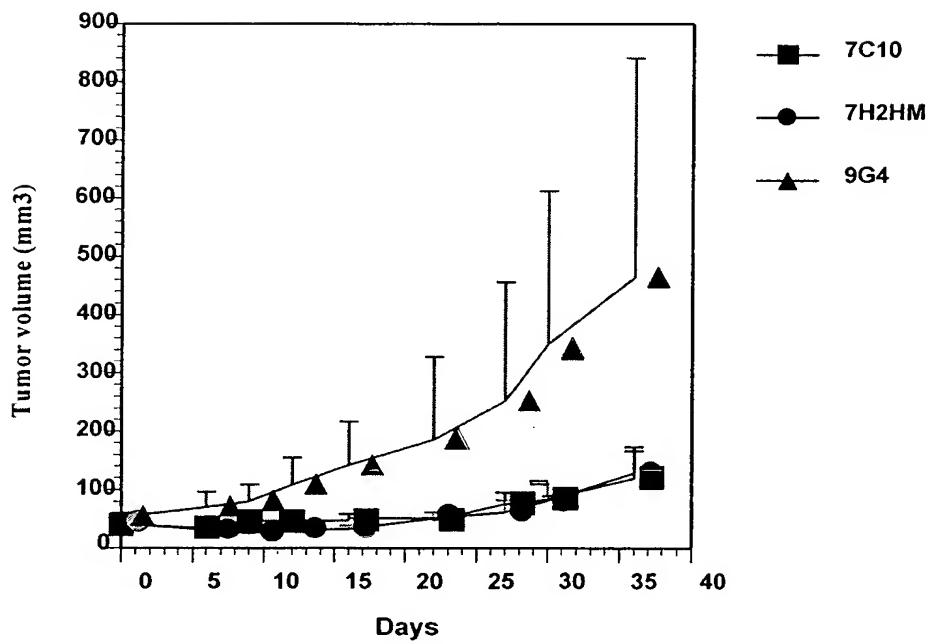


FIGURE 34B

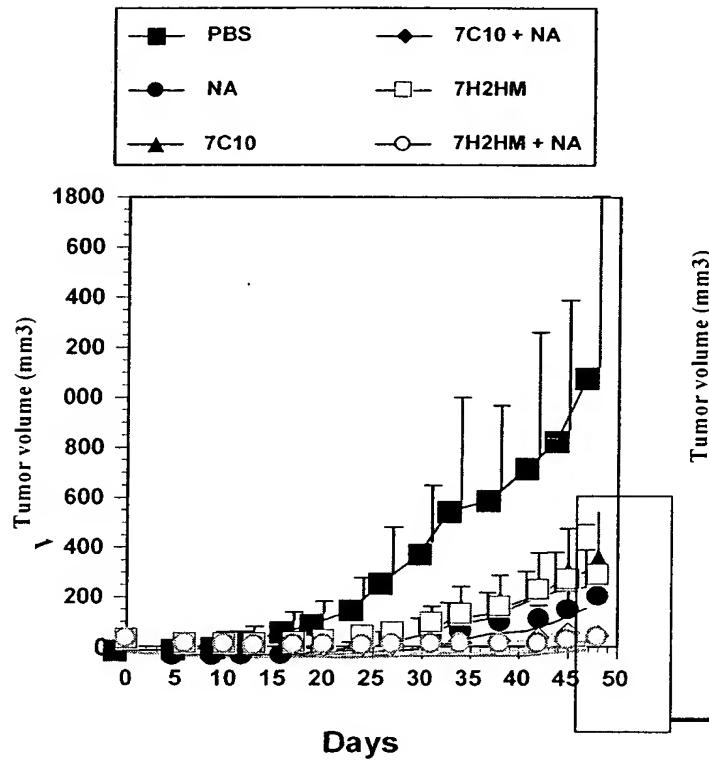


FIGURE 35A

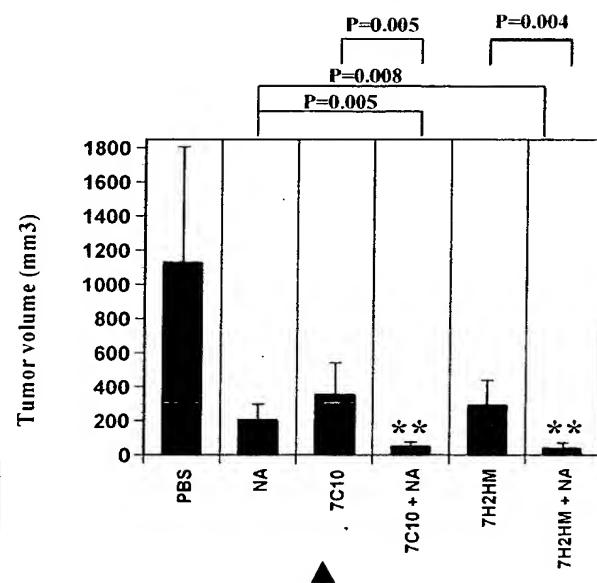


FIGURE 35B

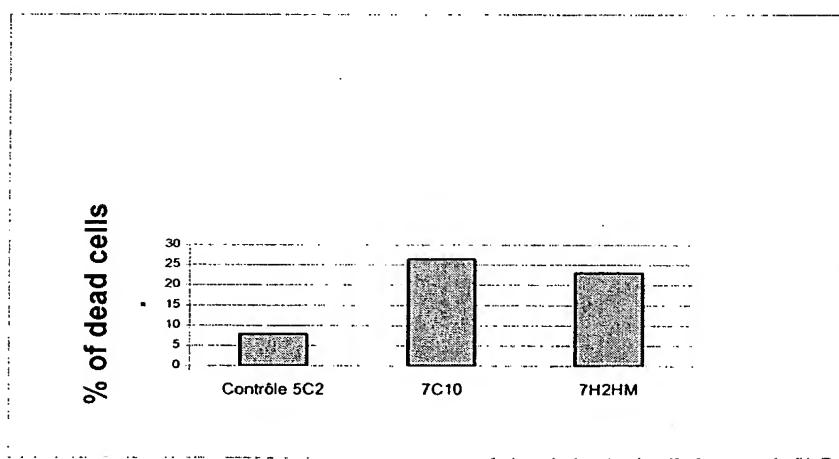


FIGURE 36

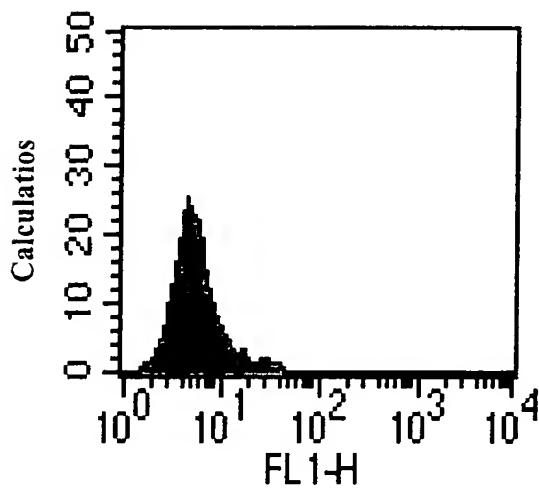


FIGURE 37A

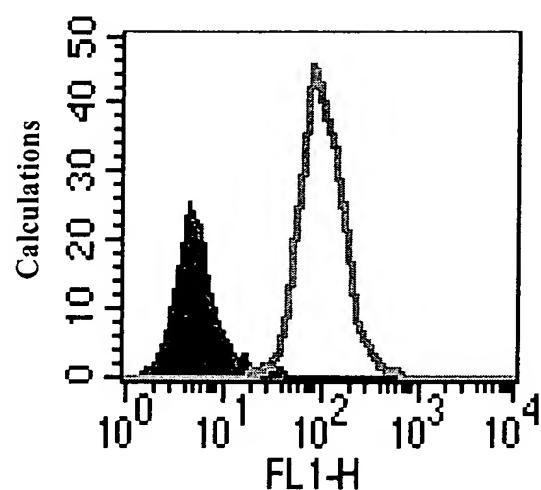


FIGURE 37B

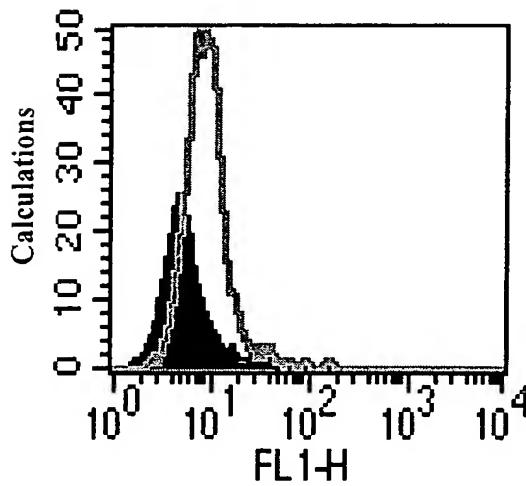


FIGURE 37C

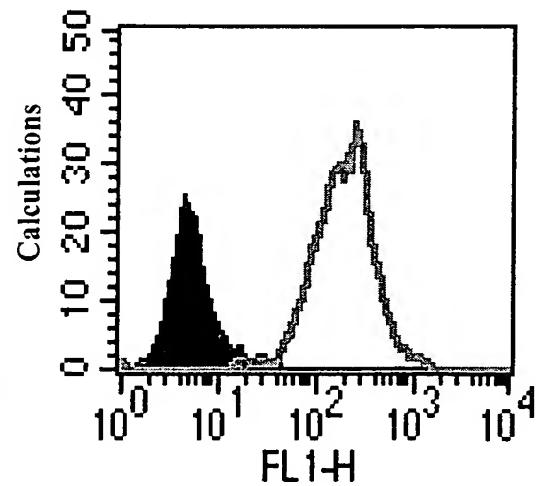


FIGURE 37D

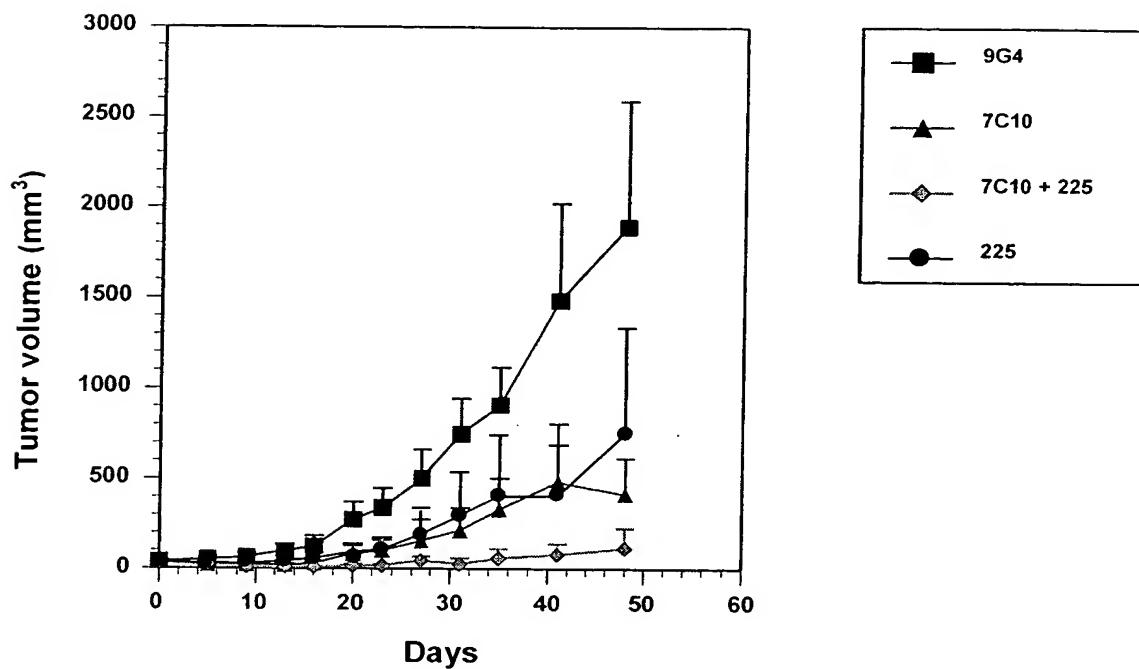


FIGURE 38

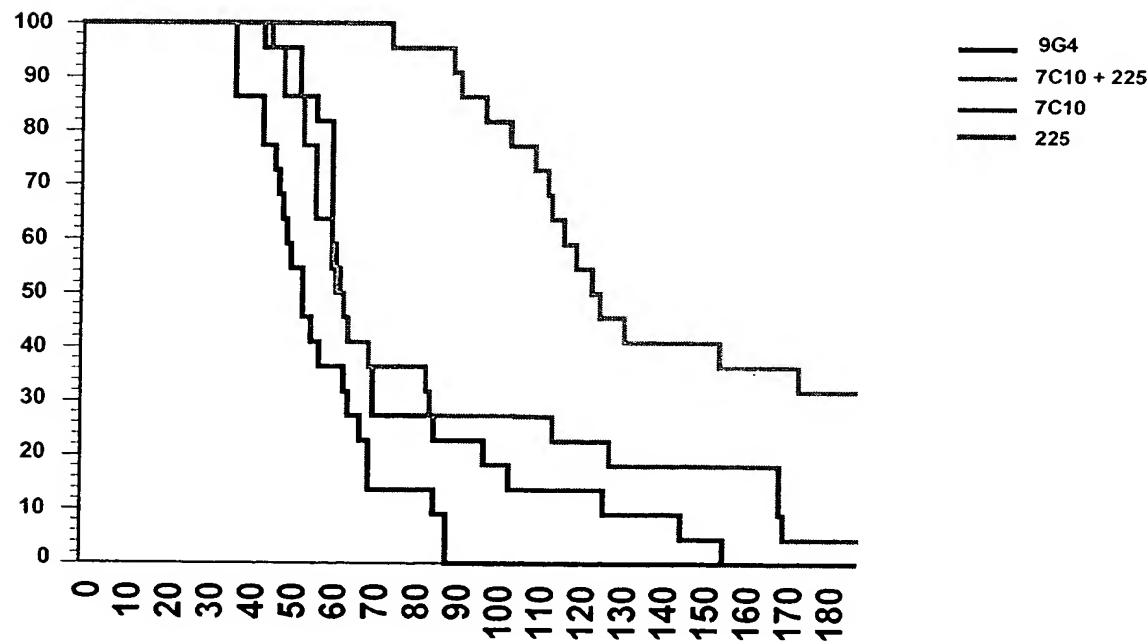


FIGURE 39

FIGURE 40A

IGF-I 50 ng/ml

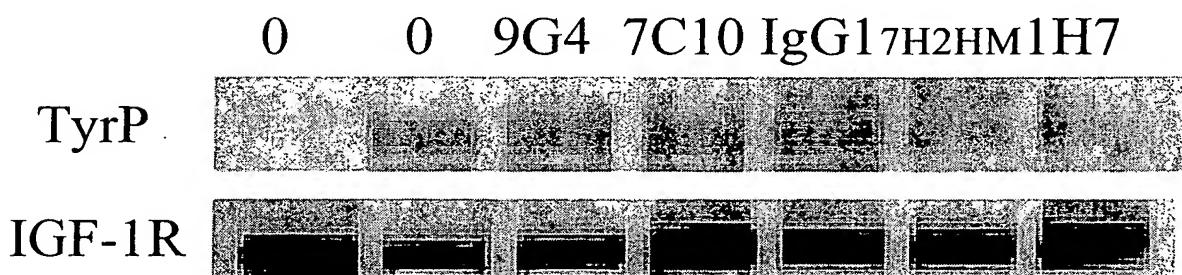


FIGURE 40B

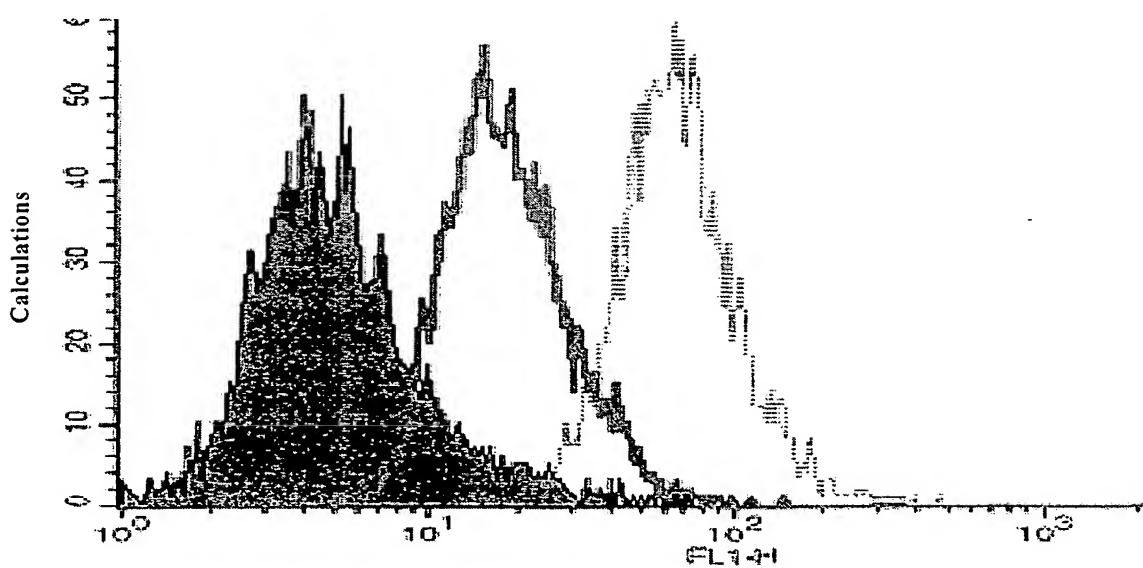
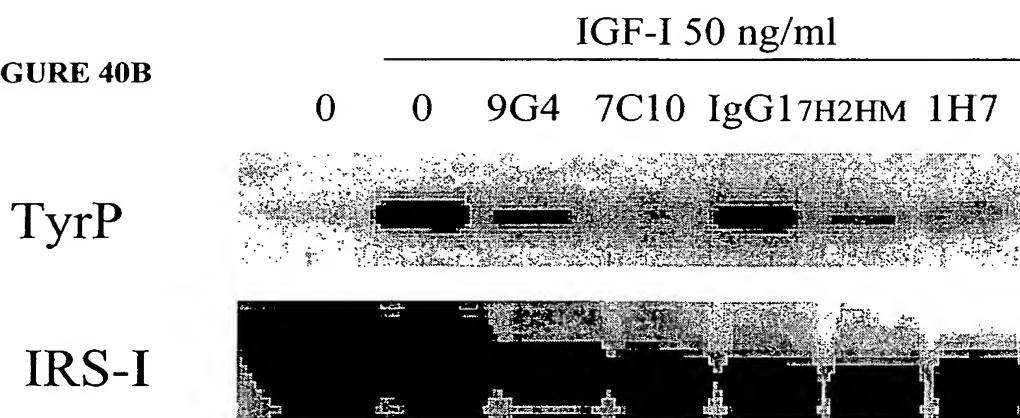
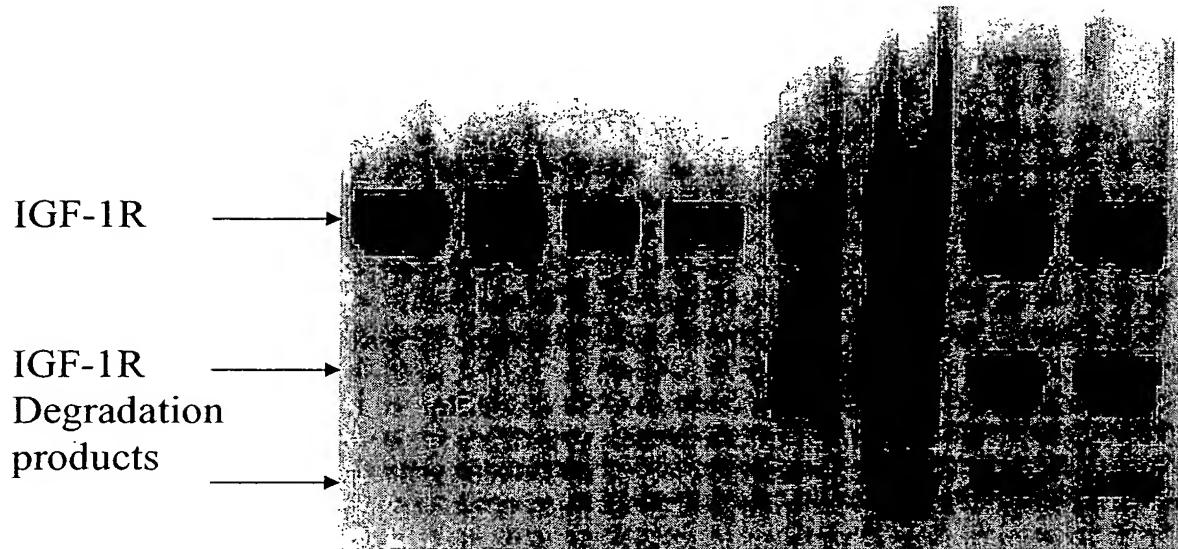


FIGURE 41



Incubation time	5	3	2	1	5	3	2	1
37°C (hours)	9G4 + IGF-I				7C10 + IGF-I			

FIGURE 42A

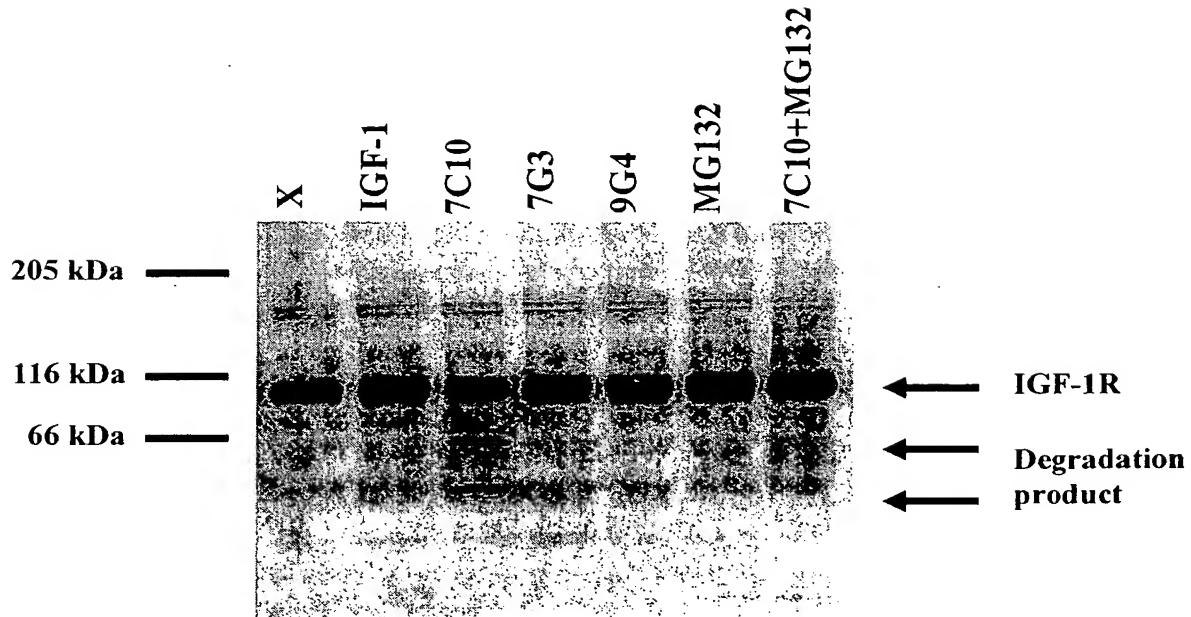


FIGURE 42B

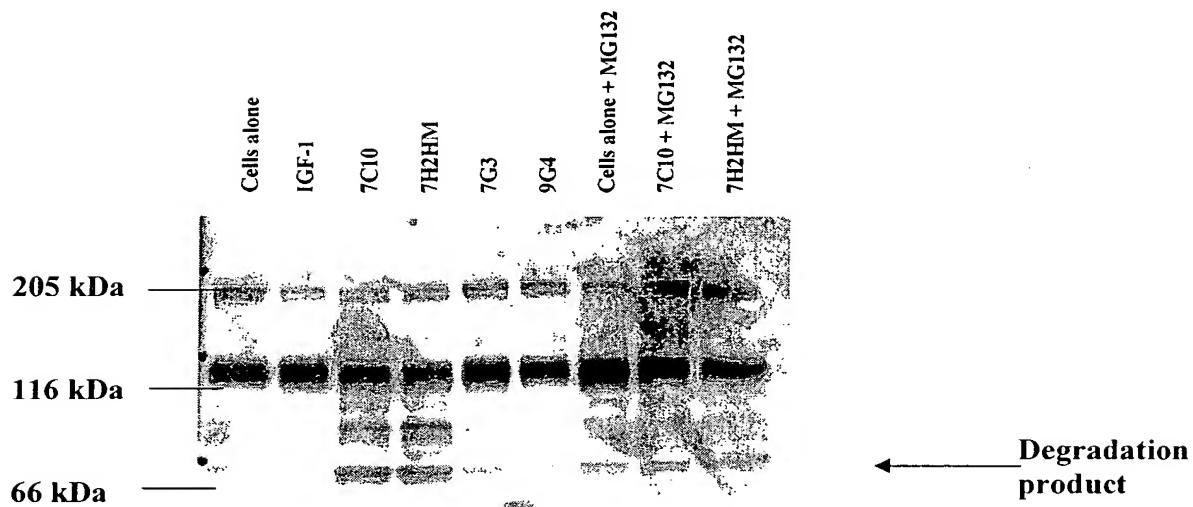


FIGURE 42C

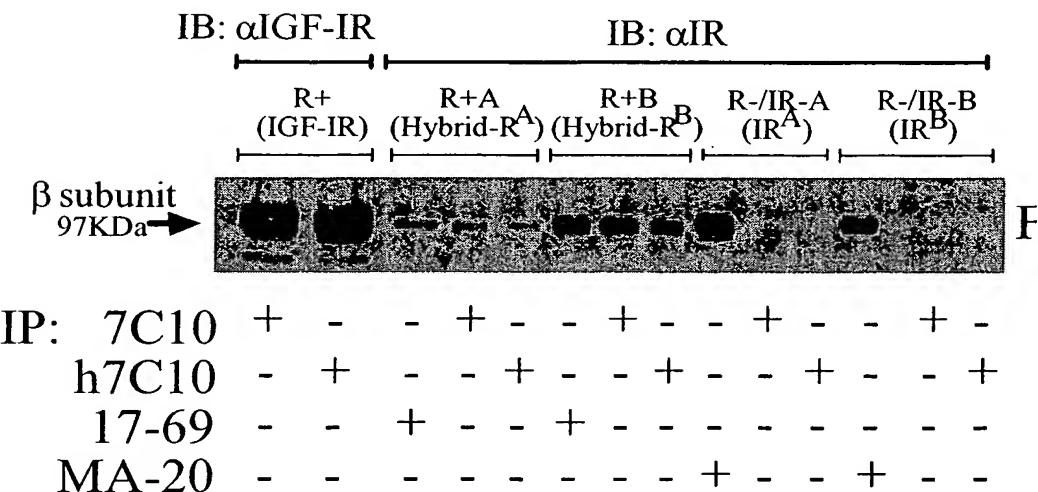


FIGURE 43A

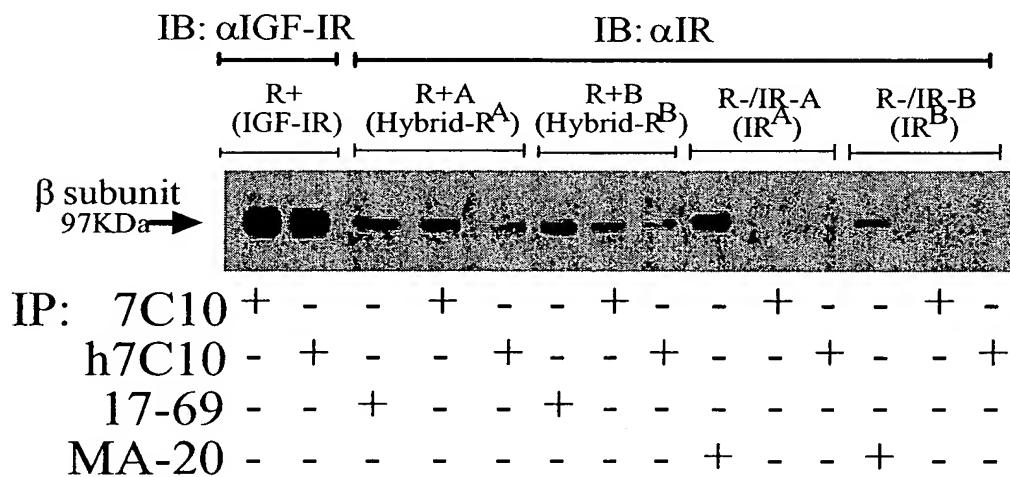


FIGURE 43B

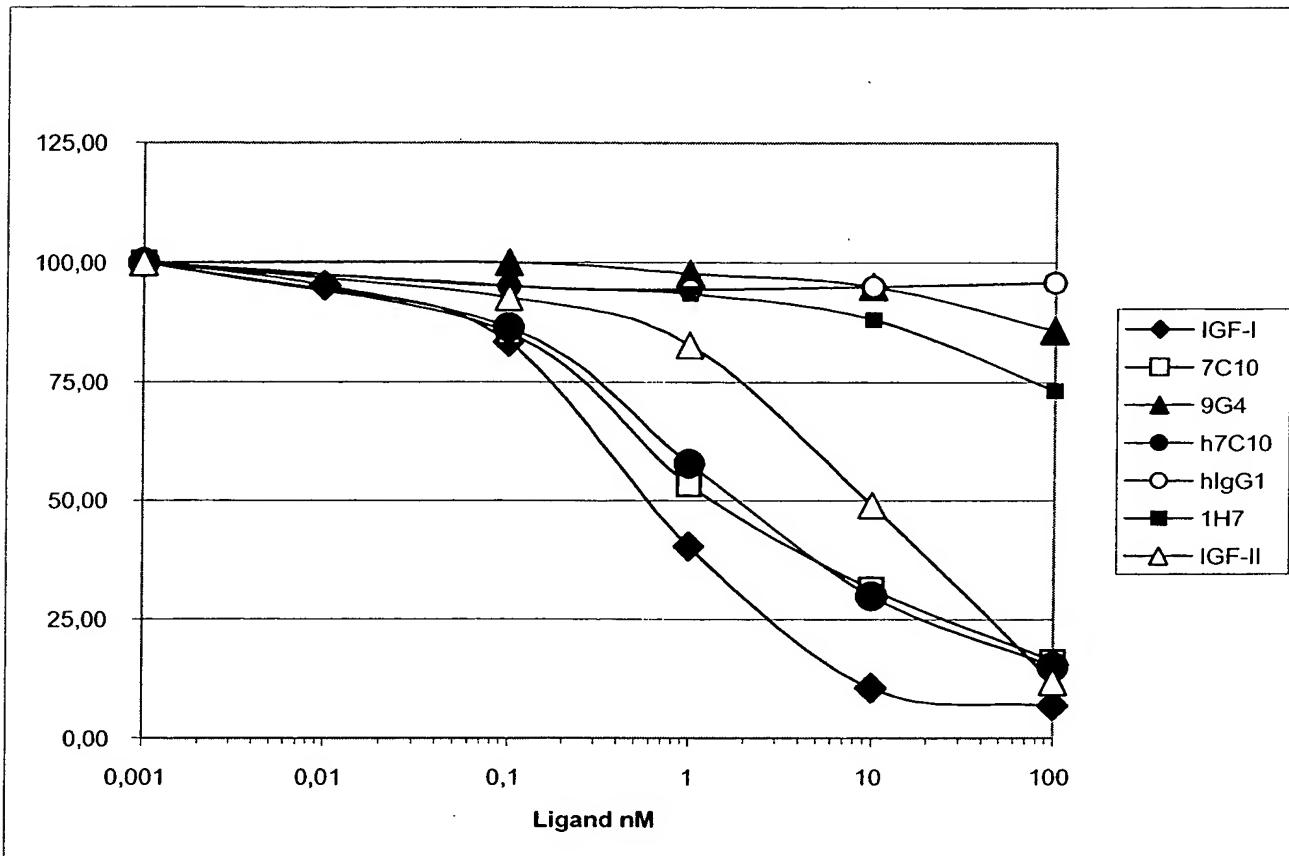


FIGURE 44

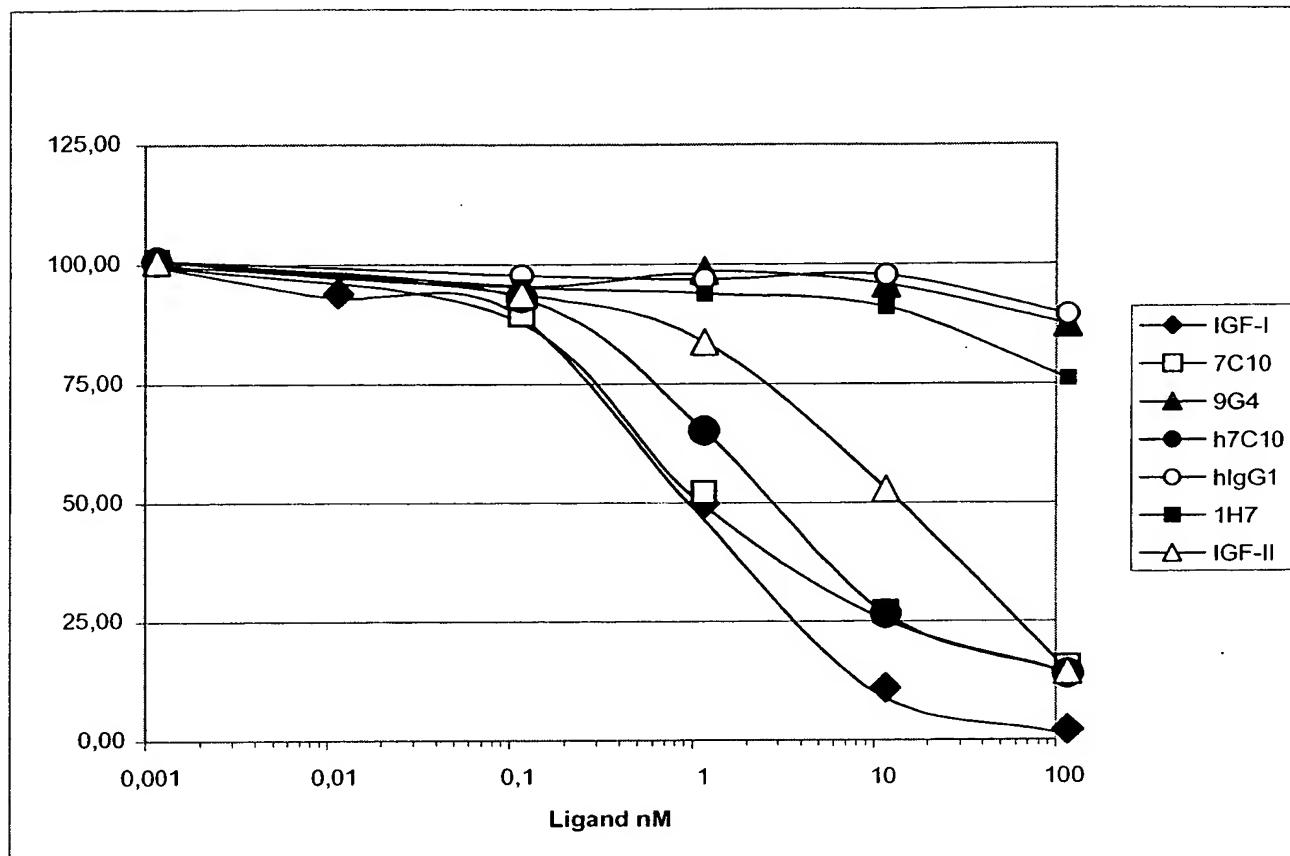


FIGURE 45

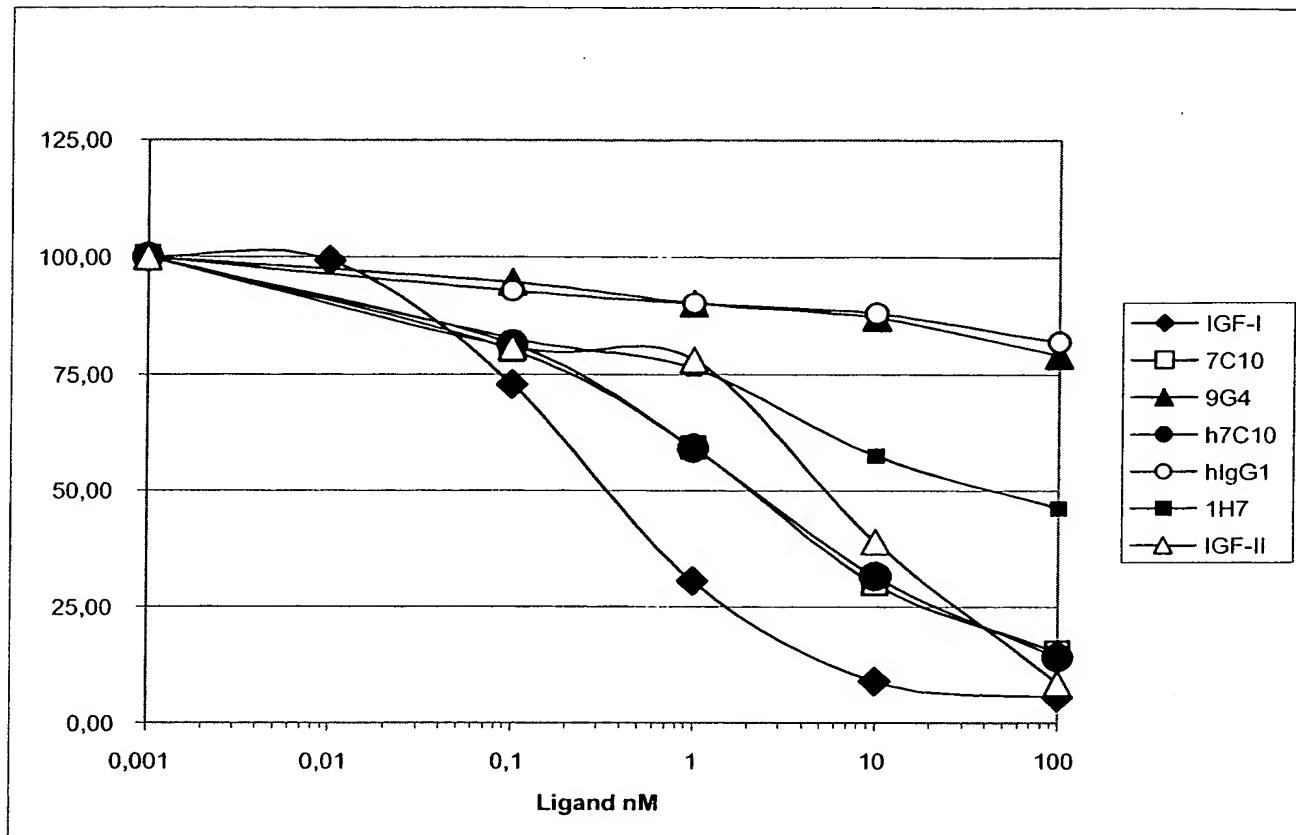


FIGURE 46

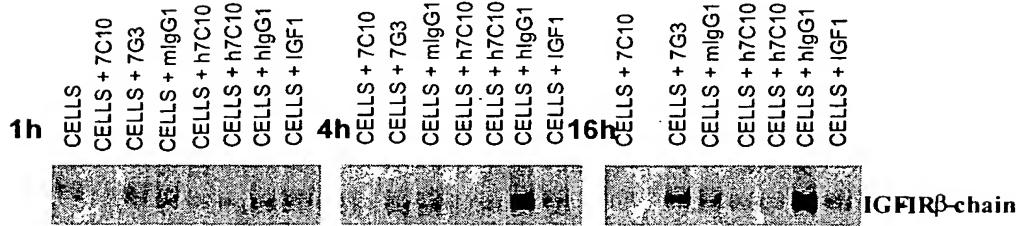


FIGURE 47A

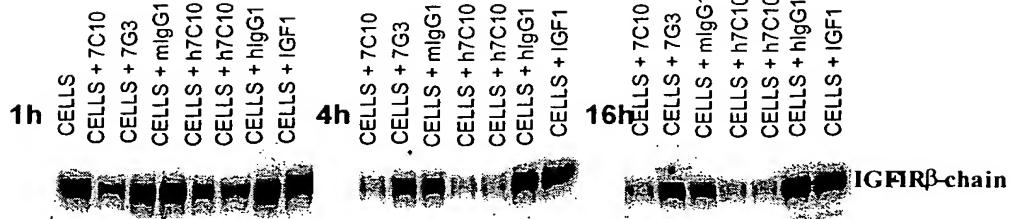


FIGURE 47B

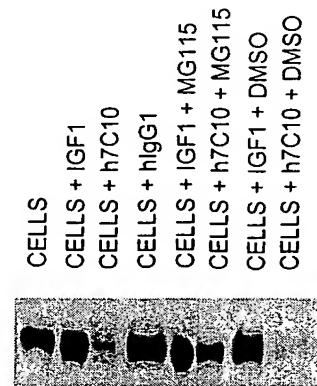


FIGURE 48

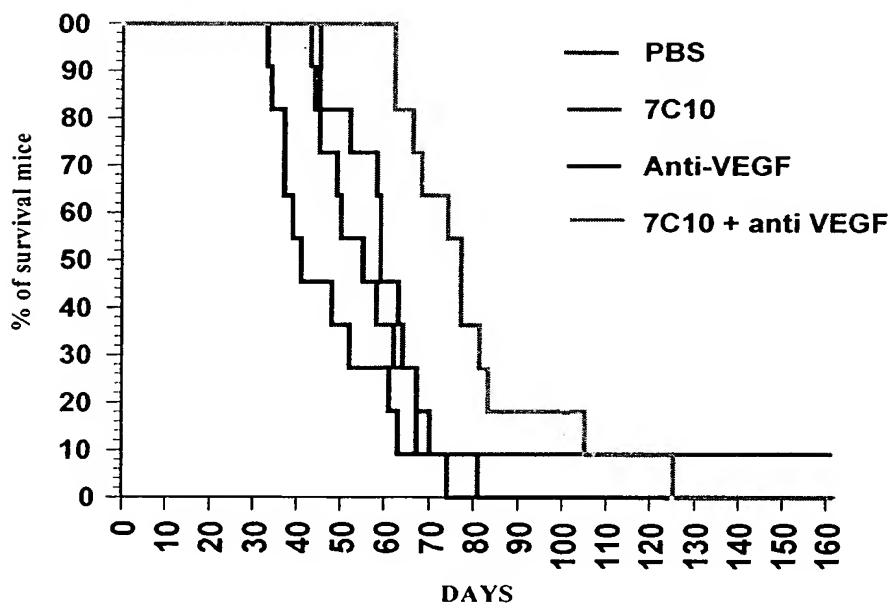


FIGURE 49

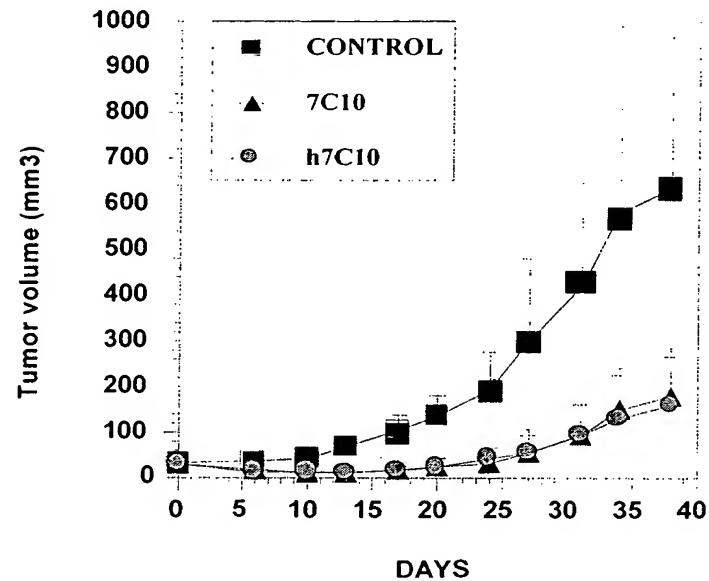


FIGURE 50

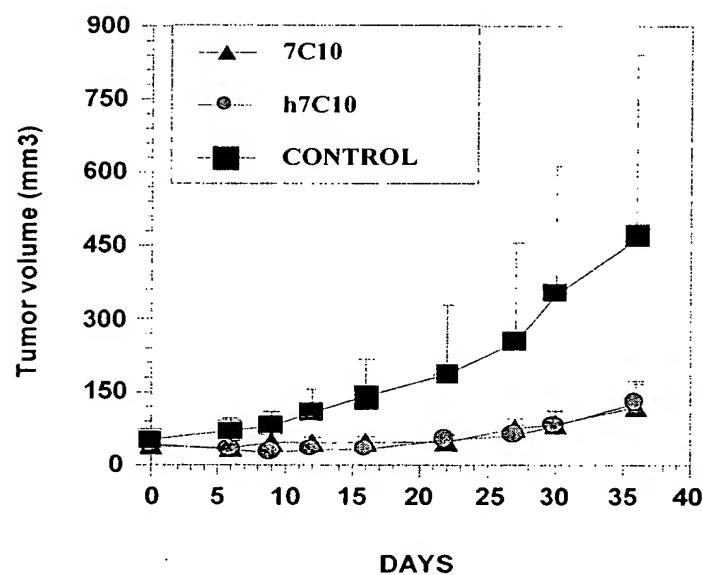


FIGURE 51

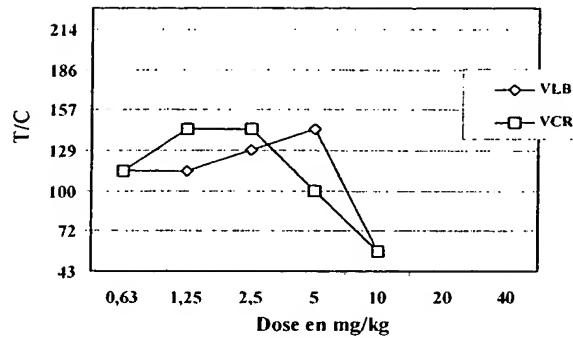


FIGURE 52

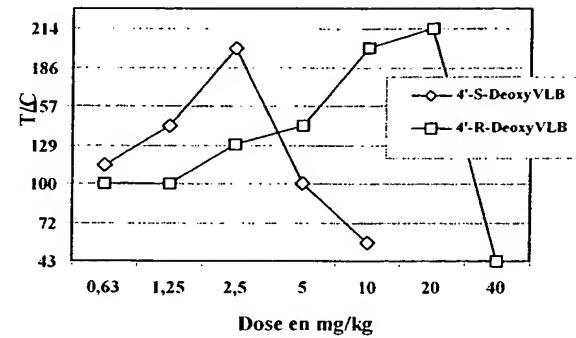


FIGURE 53

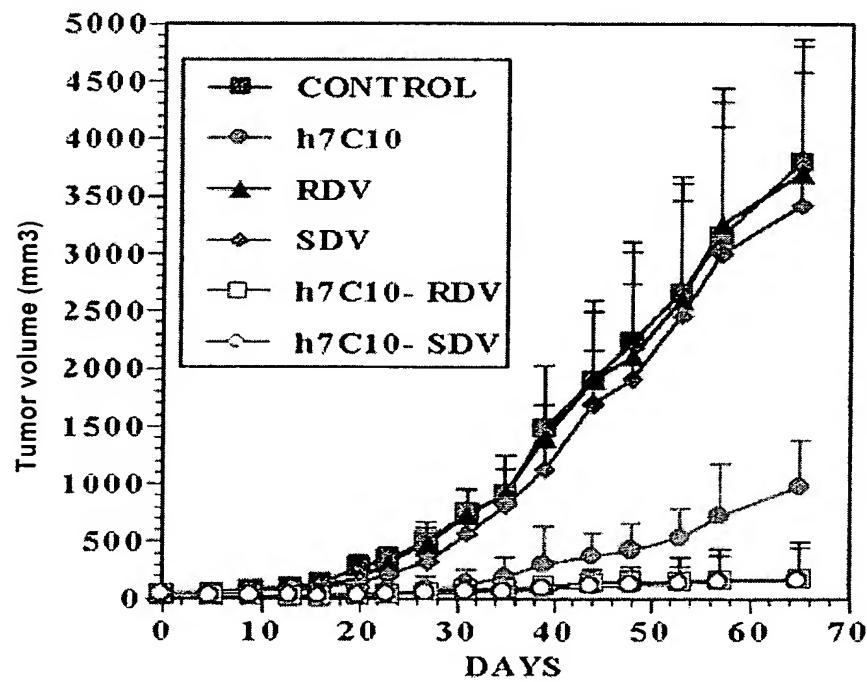


FIGURE 54

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